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STUDY OF STAPHYLOCOCCIC INFECTIONS OCCURRING ON A SURGICAL SERVICE

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Two 60-bed general surgery wards were compared as to the incidence of staphylococcic infections. In one ward, only routine precautions were taken against the spread of infections. The other ward was treated as nearly as possible like an isolation unit, with special bedding, dressing carts, and other facilities. Of 74 patients who acquired staphylococcic hospital infections during the one-year period, 41 were in the latter ward, and the semi-isolation techniques that had been used were found completely inadequate for the control of staphylococcic infections on surgical wards. Valuable data were obtained by culturing the organisms and classifying them according to coagulase reaction, antibiotic resistance, and bacteriophage type. The withdrawal of a given antibiotic for eight months was not sufficient to affect the antibiotic-resistance of prevailing strains, probably because the drugs used in any given hospital were but a fraction of those used in the community from which the patients came.

IN RECENT years increasing numbers of reports have appeared in the literature in regard to the seriousness of hospital acquired staphylococcic infections, the resistance of these organisms to the antibiotic drugs in common use, and the application of the bacteriophage-typing technique for determining the relationship of cultures from different sources.[1]

Our attention was first called to this problem while we were attempting to evaluate the cause of ever increasing numbers of cases of staphylococcic enteritis occurring on surgical wards.[1b] Although we had not experienced an actual outbreak of surgical staphylococcic infections, we were aware of the presence of sporadic cases. On this basis we decided to investigate the source of these infections, focusing our attention on the staff and personnel carrier as a potential source of cross infection, and to determine, if possible, ways and means of preventing the dissemination of Staphylococcus pyogenes var. aureus on the surgical wards.

Methods and Materials

In order to evaluate the possible benefits of simple semi-isolation techniques as a means of controlling spread of cross infection, two general surgery wards of 60 beds each, nearly identical in

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physical structure and situated one above the other, were selected for study. One was established as a study ward, the other as a control ward. In the former, private and semiprivate rooms at one end were divided from the ward proper by double doors. This area was equipped with special bedding, dressing cart, utensils, and hand washing facilities and was as far as possible established as an isolation unit.

All patients who were admitted with infections and those who developed infections during hospitalization on the study ward were placed in this area. Personnel caring for these patients wore caps, gowns, masks, and gloves, and strict aseptic technique was used when dressings were being changed. However, the same personnel were responsible for the care of patients on the remainder of the ward, which included seven-bed rooms divided into admission and postoperative rooms. On the control ward, precautions other than those routinely used were not employed. A continuous record of each patient, in relation to time, place, contact with other patients, and personnel caring for him, was kept throughout the study period.

TABLE 1.—*Phages of Four Groups of Staphylococci and Miscellaneous Groups (Blair) and Phage Patterns Most Commonly Occurring in Our Study*

Group	Characteristic Phages	Common Phage Patterns
I	29, 52, 52A, 79	52
II	3A, 3B, 3C, 55, (39), (52B)	3C
III	6, 7, 42E, 47, 53, 54, 70, 73, 75, 77, (42B), (VA4)	53/VA4, 44A, 7, 47/53/54/77/VA4, 77
IV	42D	
Miscellaneous .	44A, 81	44A
Unclassified ..		80/81, 47/42D*

* Formerly reported as 52/42B/81.

Since it has been well established that a great number of staphylococci, indigenous to our hospital, are resistant to the antibiotic drugs in common use, we decided to test the efficacy of the use of "rotational" therapy as a means of delaying or preventing the emergence of drug-resistant strains. As it has been our experience that essentially complete cross resistance occurs between the tetracycline drugs (chlortetracycline, oxytetracycline, and tetracycline) in vitro, we decided to withdraw the use of these drugs for a period of eight months and restrict their use to special requests only. Due to complete cross resistance between these drugs in vitro, they will be referred to as "the tetracyclines" and results reported accordingly.

Bacteriological Procedures.—Nasopharyngeal and rectal cultures were made on a monthly basis of members of the personnel and staff of the two surgical wards under study and the operating suite, and whenever possible on patients on admission, prior to surgery, and on the fourth postoperative day. Stomach and intestinal lumina were cultured at the time of surgery and, in cases of infection, cultures were obtained until the infection had subsided.

All staphylococci isolated were tested for their ability to produce coagulase, either by the use of the biochemical method, with use of Bacto-Mannitol salt agar and/or by their ability to clot citrated human plasma.

Drug susceptibility of pure cultures was determined by the disk-plate method, with use of Sensi-Discs exclusively. The concentrations used were as follows: penicillin and bacitracin, 2 units per milliliter respectively; dihydrostreptomycin, 10 mcg. per milliliter; novobiocin, 30 mcg. per milliliter; and neomycin, chlortetracycline, oxytetracycline, tetracycline, and chloramphenicol, 5 mcg. per milliliter respectively. Strains inhibited by these respective concentrations were classified as "sensitive"; those showing a zone of inhibition of growth of 2 mm. or less were classified as "resistant."

The technique of bacteriophage typing was used to determine the relationship of cultures from different sources. Twenty-five staphylococcic phages were obtained through the courtesy of Dr. John E. Blair and stock cultures and phages were accomplished by the method of Blair and Carr [2] and Blair.[3] Only strong lytic reactions (50 plaques or more) were taken into consideration in reporting of results. Table 1 illustrates the phages of the four broad groups of staphylococci and the miscellaneous groups and the phage patterns most commonly occurring in our study.

Results

During the one-year study period, 74 patients acquired hospital infections caused by coagulase-positive, phage typable staphylococci; contacts were established in 42 of these cases. Forty-one of the patients were located on the study ward and 33 on the control ward. Of cases of cross infection, 24 were located on the study ward and 18 on the control ward. Eleven patients acquired a carrier state at one time or another during their hospitalization.

Included in the hospital acquired infections were 9 preoperative infections (as determined by cultures taken either prior to or at the time of surgery); 44 postoperative wound infections; 7 postoperative complications of other types; and 14 nonsurgical cutaneous infections. Fifty-one patients acquiring infections during their postoperative period indicate an infection rate of 4% (1,350 operations).

Twenty-four patients had infections at time of admission to the wards and 28 patients were nasopharyngeal and/or fecal carriers on admission.

In regard to the staff and personnel of the three study units, carrier rates were as follows: study ward, 34%; control ward, 38%; and operating suite, 40%. Of a total of 114 individual carriers, 49 were nasopharyngeal, 36 were fecal, and 29 were simultaneous nasopharyngeal and fecal carriers. Based

on the results of phage typing, 11 of these individuals were "persistent" carriers; that is, they harbored staphylococci of the same phage pattern for a minimum of five consecutive months. Their distribution was as follows: study ward, three; control ward, four; and operating suite, four.

We were unable to demonstrate any significant change in rate of incidence of staphylococci resistant to the three tetracycline drugs, due to a withdrawal of their use for a period of eight months. This phase of our investigation will be reported in detail in a subsequent paper.

One thousand five hundred forty-seven strains of Staph. pyogenes var. aureus were isolated from a variety of 3,632 clinical specimens cultured for this organism. Of these, 56% were coagulase-negative, of which 36% were resistant to penicillin, 19% to erythromycin, 38% to dihydrostreptomycin, 38% to the tetracyclines, and 18% to chloramphenicol. Forty-four per cent of the strains were coagulase-positive, with incidence of drug resistance as follows: 42% to penicillin, 16% to erythromycin, 36% to dihydrostreptomycin, 30% to the tetracyclines, and 17% to chloramphenicol. Strains resistant to bacitracin (12%), neomycin (20%), and novobiocin (17%) were infrequently encountered and therefore will not be further mentioned.

Of 515 strains subjected to phage typing with the 25 phages used, 27% were untypable and 82% were typable with one or more of the phages used. Of the latter, 56% were typable with phages used at the routine test dilution and 15% with phages used at a 1:10 dilution.

Incidence of drug resistance among the untypable strains was 63%, with 26% resistant to penicillin, 21% to erythromycin, 38% to dihydrostreptomycin, 33% to the tetracyclines, and 35% to chloramphenicol. Incidence of drug resistance among the typable strains was 59% with individual drug resistance as follows: 43% to penicillin, 15% to erythromycin, 35% to dihydrostreptomycin, 32% to the tetracyclines, and 15% to chloramphenicol. Of the resistant typable strains, 30% were resistant to a single drug and 65% were multiple resistant.

Table 2 illustrates the incidence of phage patterns in relation to antibiotic susceptibility (372 strains; 33 patterns). Our most commonly occurring patterns were 53/VA4, 44A, 7, 47/42D, 47/53/54/77/VA4, 77, 80/81, 52 and 3C, and these staphylococci accounted for 86% of the total number of strains.

Incidence of drug resistance in the above patterns was 63% with drug resistance as follows: 46% to penicillin, 16% to erythromycin, 37% to dihydrostreptomycin, 35% to the tetracyclines, and 16% to chloramphenicol. Thirty-three per cent of the remaining staphylococci (falling into 24 patterns) were drug resistant.

Table 3 illustrates the relationship of patients with hospital acquired infections and those having infections on admission to the distribution of phage patterns.

Hospital Acquired Infections.—Of 74 patients having hospital acquired infections, 83% were caused by staphylococci of eight of our commonly occurring patterns (53/VA4, 44A, 7, 47/53/54/77/-VA4, 77, 47/42D, 80/81, and 3C). However, 39 of the 42 cases of cross infection were caused by staphylococci of the first five patterns. Therefore,

TABLE 2.—*Relation of Incidence of Phage Patterns to Antibiotic Susceptibility (372 Strains)*

Phage Pattern	Total No. of Strains	Total No. Resistant	No. Resistant to*				
			P	E	DS	T	Ch
53/VA4†	105	93	76	32	73	54	31
44A	18	27	16	6	15	14	4
7‡	44	20	8	4	4	2	12
47/42D§	37	14	11	0	3	7	1
47/53/54/77/VA4†	30	16	15	6	11	7	3
80/81	16	14	10	2	4	14	1
77	12	7	3	3	4	6	3
52¶	12	6	6	1	3	4	0
3C‖	11	4	2	0	2	2	1
47/81	4	2	1	0	1	0	0
52A/81	3	3	3	0	2	2	1
7/47/53/54/75	3	2	1	1	2	1	1
47/53/54/77/VA4/81	2	2	0	0	2	2	0
81	2	2	2	0	1	0	0
77/44A	2	2	2	0	1	1	0
47/53/77/VA4/44A	2	2	2	0	1	1	0
52/79/44A	2	1	1	1	1	1	0
79	1	1	1	0	1	0	0
3/53	1	1	1	0	0	0	0
7/VA4/44A	1	1	1	0	1	1	0
52A	6	0	0	0	0	0	0
29/44A	5	0	0	0	0	0	0
47	4	0	0	0	0	0	0
42D	4	0	0	0	0	0	0
79	4	0	0	0	0	0	0
3A/44A	3	0	0	0	0	0	0
42D/44A	2	0	0	0	0	0	0
3A/3B/3C/55	1	0	0	0	0	0	0
7/47/53/73	1	0	0	0	0	0	0
6/73	1	0	0	0	0	0	0
55	1	0	0	0	0	0	0
42B	1	0	0	0	0	0	0
29/47	1	0	0	0	0	0	0
Grand totals	372	220	162	56	132	119	58
% resistant		59	43	15	35	32	15

* P = penicillin; E = erythromycin; DS = dihydrostreptomycin; T = tetracyclines; and Ch = chloramphenicol.
† May be joined by 77 or 47.
‡ May be joined by 77.
§ May be joined by 53, VA4, or 53/VA4.
¶ May be joined by 6.
‖ May be joined by 52A.
May be joined by 3A, 3B, or 55.

our predominant or major hospital patterns were 53/VA4, 44A, 7, 47/53/54/77/VA4, and 77.

In regard to the 28 cases of cross infection of postoperative wounds, of the five predominant patterns, 53/VA4 staphylococci were responsible for 13; 44A for 6; pattern 7 for 3; 47/53/54/77/VA4 for 2; and pattern 77 for 2.

Admission Infections.—Of 24 patients having infections on admission, 17 were caused by staphylococci of six of our commonly occurring patterns (53/VA4, 44A, 47/53/54/77/VA4, 77, 80/81, and 3C). However, 10 of these cases were caused by

staphylococci included in four of our predominant patterns. Table 4 illustrates incidence of phage patterns and their antibiotic susceptibilities in relation to the three groups of persons studied.

TABLE 3.—*Incidence of Patients with Hospital Acquired Infections and Patients with Infections at Time of Admission in Relation to Distribution of Phage Pattern*

Phage Pattern	Pre-operative Infections	Post-operative Infected Wounds	Other Post-operative Infections	Non-operative Cutaneous Infections
Number of Cases of Hospital Acquired Cross Infections (42)				
53/VA4	1	13	2	1
44A	2	6	1	1
7	1	3	1	0
47/53/54/77/VA4	0	2	0	1
77	1	2	0	1
47/42D	0	1	0	0
80/81	0	0	0	1
52A/81	0	1	0	0
Totals	5	28	4	5
Hospital Acquired Infections Lacking Demonstrable Contacts (32)				
53/VA4	0	3	1	2
7	1	1	1	0
77	0	1	0	0
47/42D	0	2	1	3
80/81	0	1	1	1
3C	0	2	0	0
10 less common patterns*	0	5	0	6
Totals	1	15	4	12
Number of Cases of Admission Infections (24)				
53/VA4	1	0	1	1
44A	0	0	0	2
47/53/54/77/VA4	0	0	0	4
77	0	0	0	1
80/81	0	0	0	4
3C	0	0	0	3
5 less common patterns†	1	2	0	4
Totals	2	2	1	19

* Patterns responsible for five postoperative wound infections: 47, 6/78, 42B, 52B, and 3A/44A.
† Patterns responsible for two postoperative wound infections: 52/79/44A and 47/81.

Group A represents 122 strains (24 patterns) isolated from cultures from a wide variety of clinical sources from 102 inpatients. Included in this group are 42 patients with hospital acquired cross infections, 32 patients with hospital acquired infections but lacking demonstrable contacts, and 11 patients who acquired a carrier state sometime during their hospitalization. Staphylococci of our five major hospital patterns (53/VA4, 44A, 7, 47/53/54/77/VA4, and 77) accounted for 70% of the total number, and were responsible for 39 of the 42 cases of cross infection.

Incidence of drug resistance in group A was 65%, with 48% of the strains resistant to penicillin, 19% to erythromycin, 45% to dihydrostreptomycin, 44% to the tetracyclines, and 25% to chloramphenicol.

Group B represents 178 strains isolated from nasopharyngeal and/or fecal carriers from the staff and personnel of the study and control wards and from the operating suite. Of these, 152 were nasopharyngeal isolations and 26 were fecal. Staphylococci of our five major hospital patterns accounted for 68% of the total number. Pattern 53/VA4 staphylococci were harbored by 16 carriers, 44A by 12, pattern 7 by 10, 47/53/54/77/VA4 by 7, and pattern 77 by 2. Staphylococci of 53/VA4, 44A, and 7 were harbored by both nasopharyngeal and fecal carriers, whereas those of the remaining patterns were harbored by the former only.

Incidence of drug resistance in group B was 56%, with 38% of the strains resistant to penicillin, 15% to erythromycin, 26% to dihydrostreptomycin, 22% to the tetracyclines, and 10% to chloramphenicol.

Comparison of groups A and B shows that a close correlation exists between phage patterns of staphylococci cultured from patients with hospital acquired cross infections and those exhibited by carriers among the staff and personnel. Although we encountered nine nasopharyngeal carriers among the inpatients, only one played a role in cross infection. Of our predominant patterns, 53/VA4 and 47/53/54/77/VA4 were the only two associated with these patients. Other patient-to-patient contacts, in cross infections, will be discussed later.

TABLE 4.—*Incidence of Phage Patterns and Their Antibiotic Susceptibilities in Relation to the Three Groups of Persons Studied*

Group	Phage Pattern	Total No. of Strains	Total No. Resistant	No. Resistant to* P	E	DS	T	Ch
A	53/VA4	42	36	31	15	32	25	13
Inpatient strains	44A	16	10	7	3	6	8	3
	7	14	9	1	2	2	2	9
	47/42D	10	4	4	0	3	4	1
	47/53/54/77/VA4	9	3	3	2	2	2	1
	80/81	4	4	4	0	0	4	0
	77	4	2	1	2	2	2	2
	52	1	1	1	0	1	1	0
	3C	2	2	2	0	0	0	0
	Less common patterns	20	9	5	0	7	6	2
Totals		122	80	59	24	55	54	31
% resistant			65	48	19	45	44	25
B	53/VA4	50	45	34	14	29	23	13
Carrier strains	44A	28	13	7	3	7	4	0
(staff and	7	26	9	5	2	1	0	3
personnel)	47/42D	22	10	7	0	0	3	0
	47/53/54/77/VA4	11	8	7	1	5	1	0
	80/81	3	2	0	1	0	2	0
	77	6	4	2	0	2	3	1
	52	11	5	5	1	2	3	0
	3C	2	1	0	0	1	1	1
	Less common patterns	19	1	1	0	0	0	0
Totals		178	98	68	22	47	40	18
% resistant			56	38	15	26	22	10
C	53/VA4	13	12	11	3	12	6	5
Admission strains	44A	4	4	2	0	2	2	1
	7	4	2	2	0	1	0	0
	47/42D	5	0	0	0	0	0	0
	47/53/54/77/VA4	10	5	5	3	4	4	2
	80/81	9	8	6	1	4	8	1
	77	2	1	0	1	0	1	0
	52	0	0	0	0	0	0	0
	3C	7	1	0	0	1	1	1
	Less common patterns	18	8	8	1	4	2	0
Totals		72	41	34	9	28	24	10
% resistant			56	47	12	38	33	13

* P = penicillin; E = erythromycin; DS = dihydrostreptomycin; T = tetracyclines; and Ch = chloramphenicol.

Group C represents 72 strains (21 patterns) isolated from various clinical sources from 24 patients having infections at the time of admission and from 28 nasopharyngeal and/or fecal admission carriers. Forty-five per cent of these staphylococci fell into our five predominant patterns (53/VA4, 44A, 7, 47/53/54/77/VA4, and 77).

Incidence of drug resistance in this group was 56%, with 47% of the strains resistant to penicillin, 12% to erythromycin, 38% to dihydrostreptomycin, 33% to the tetracyclines, and 13% to chloramphenicol.

It is obvious from the foregoing report that our predominating "endemic" pattern was 53/VA4. This pattern included 105 strains, or more than twice as many strains as those occurring in any other single pattern. These staphylococci were responsible for 13 of 28 cases of hospital acquired postoperative cross-wound infections. They comprised 30% of all strains isolated from infected lesions from patients having hospital acquired infections and 30% of all strains harbored by the staff and personnel, including a total of 16 carriers (5 of whom were persistent carriers). In addition they were also harbored by six inpatient and three admission patient carriers. Eighty-seven per cent of the 53/VA4 strains were drug resistant and, of these, 84% were multiple resistant. Furthermore, 46% of all cultures resistant to penicillin and 50% of all cultures resistant to the three tetracycline drugs were of this pattern.

For the purpose of comparison, our second most commonly occurring pattern was 44A, which included 48 strains. These staphylococci were responsible for 6 of the 28 cases of hospital acquired postoperative cross infections of wounds. They comprised 12% of all strains isolated from infected lesions from patients with hospital acquired infections, and 15% of all strains harbored by the staff and personnel, including a total of 11 carriers (2 of whom were persistent carriers). In addition they were harbored by one admission carrier. Fifty-six per cent of the 44A staphylococci were drug resistant and of these, 11% were multiple resistant.

In the 42 cases of hospital acquired cross infections, results indicate that 13 infections had their origin in the operating suite; contacts included two surgeons, five anesthetists, two scrub nurses, and two aides. Twenty-four cases apparently originated from contacts with ward staff and personnel carriers. These included two surgeons (including one listed in the above category), five nurses, and three aides (table 5).

Of 17 cases of cross infection due to 53/VA4 staphylococci, results of phage typing indicate that 2 had their origin in operating suite and 15 in the wards. Of the latter, 10 originated from a single contact of the study ward and 5 from a single contact on the control ward. Both contacts were ward nurses and both were persistent nasopharyngeal carriers and transient fecal carriers of the organism in question.

Five cases of cross infection were traced to patient-to-patient contacts. Four contacts had open cutaneous lesions and one was a nasopharyngeal carrier. Pattern 53/VA4 staphylococci were not concerned in these cases; incriminating patterns were 44A, 47/53/54/77/VA4, 80/81, and 52A/81 (table 5).

Seven cases of auto-infection were included in the group of 32 hospital acquired infections lacking demonstrable contacts. The responsible staphylococci were included in patterns 53/VA4 (2 cases), 3A/44A, 80/81 (2 cases), 52A/81, and 3C.

Comment

Results of this investigation indicate that our infection rate (4%) is lower than that reported by Jeffrey and Sklaroff [1m] in a similar study (9%). Our infection rate seems favorably low, especially when we take into consideration that 38 of our 51 patients with postoperative infections had major surgery, the operations requiring two to five hours. Furthermore, all patients were males and 70% were over 50 years of age. Incidentally, 36 of these patients received antibiotic drugs prophylactically and/or therapeutically. Six patients received drugs on the latter basis, to which their respective strains were resistant in vitro.

TABLE 5.—*Professional Status of Carrier Contacts in Relation to Number of Cases of Cross Infection*

Professional Status of Carrier	No.	Cross Infection Cases, No.
Operating Suite		
Surgeons	2	2
Anesthesiologists	5	7
Scrub nurses	2	2
Aides	2	2
Study ward		
Ward surgeons	1	2
Nurses	3	12
Aides	1	1
Control ward		
Ward surgeons	1	1
Nurses	2	6
Aides	1	2
Patient-to-patient contacts	5	5

Since a greater number of cross infections occurred on the study ward than occurred on the control ward, we conclude that the practice of semi-isolation techniques was completely inadequate for the control of spread of staphylococcic infections on surgical wards.

The results of the use of rotational therapy as a means of delaying or preventing the emergence of drug-resistant staphylococci were equally disappointing. We were unable to demonstrate that the withdrawal of the use of tetracycline drugs, for a period of eight months, in any way influenced the rate of incidence in recovery of resistant strains. This is not too surprising when one considers that the amount of those drugs used in our hospital represents but a small fraction of their use through-

out the area from which we draw patients, a premise substantiated by 33% of our admission strains being resistant to the drugs in question.

We were able to establish, by phage typing of cultures, a correlation between phage patterns of staphylococci responsible for hospital cross infections and those exhibited by staff and personnel carriers of both wards and the operating suite. In the past, much attention has been focused on the nasal and nasopharyngeal carrier as the main source of spread of infection in hospital populations.[1] However, little attention has been focused on the fecal carrier. Brodie and his associates [1e] emphasize the importance of the latter among hospitalized patients as an added potential source of infection; the authors call attention to their presence among the surgical staff and personnel. If our search for carriers had been based solely on nasopharyngeal isolations, 31% of our 114 carriers would have been completely overlooked as well as the interesting phenomenon that the nasopharyngeal carrier is frequently a simultaneous fecal carrier.

The problem of control of staff and personnel carriers remains a difficult one. We have no new ideas to offer but reemphasize the need for a diligent search for carriers on the basis of phage typing of cultures. The fact that 65% of our inpatient strains and 55% of our carrier strains were drug resistant suggests that the acquisition of these organisms by the latter group is primarily a matter of their availability within a given area. Consequently, the strict practice of aseptic techniques in the handling and care of patients should result in a lowering of carrier rate, and a subsequent reduction in the number of cross infections due to resistant staphylococci.

Although we did not encounter any cases of bacteremia in our series, four deaths were included in which coexisting staphylococcic infections were considered to be a contributing factor. Our problem concerned sporadic cases rather than an actual outbreak of staphylococcic infections. What then is the effect of such cases occurring on a surgical service? Our experience agrees with that reported by Jeffrey and Sklaroff [1m] that the primary effect is economic, brought about by prolongation of hospital stay. For example, occurrence of cross infections of postoperative wounds in 18 of our patients resulted in a total increase in hospital stay of 432 days beyond the usual time required for hospitalization, or a mean of 24 days per patient. The financial impact of such a situation is apparent.

We found little evidence to support the reasoning that inpatient nasopharyngeal carriers of coagulase-positive staphylococci serve as a potential source of cross infection. On the other hand, patients having open cutaneous lesions present a real hazard as sources of cross infection on surgical wards.

It has been frequently emphasized in the past [1f] that, in any particular hospital, the important staphylococci may belong to only a few phage patterns carried in the anterior nares or nasopharynx of the staff and personnel. Such has been our experience, the important staphylococci in our series belonging to 5 of 33 patterns. Furthermore, staphylococci of each of the five important patterns were also introduced into the wards from outside sources. Our results also indicate that staphylococci of our "predominant" or "endemic" pattern (53/VA4) were endowed with enhanced powers of communicability, infectivity, and resistance to the antibiotic drugs in common use.

The universal observation that the majority of drug-resistant staphylococci belong to broad group 3 correlates with our results. Of 220 drug-resistant strains, 62% belonged to this group. However, drug-resistant staphylococci were also encountered in each of the remaining groups.

Since 1954 the dissemination of 80/81 staphylococci in the United States has been wide and rapid. As a result, these organisms are causing particular concern throughout the country. However, the chief concern has been limited to outbreaks of infections in nurseries and in outbreaks of breast abscesses in nursing mothers. Although staphylococci of this pattern were included in our nine commonly occurring patterns, they were of little or no significance in cross infections (only 1 in 42 cases, and this a nonsurgical cutaneous infection). It is pertinent to mention that the patients from whom these particular staphylococci were recovered were all males, with the majority over 50 years of age. Thus it would seem that these strains have a special predilection for the newborn infant and nursing mothers.

It is regrettable that we were unable to subject all of our cultures of coagulase-positive staphylococci to phage typing. During the first four months of the study period, we were handicapped by lack of adequate technical assistance and subsequently lost a number of stock cultures due to contamination on refrigeration.

Conclusions

The problems of control of staff and personnel as contacts in cross infection and the prevention of emergence of drug-resistant strains have not been solved by the results of our investigation. They remain extremely difficult problems. Certainly they call for strict practice of aseptic techniques and for the conservative and intelligent use of the antibiotic drugs at our disposal.

For a better understanding of the pathology, epidemiology, and chemotherapy of hospital acquired staphylococcic infections occurring on a surgical service, it is necessary to determine the drug susceptibility and phage patterns of each strain cultured from inpatients and admission pa-
and personnel.
tients, as well as from periodic cultures of the staff

West National Avenue at 54th Street (Dr. Smith).

Mrs. Lorraine M. Kastensen and Mr. Abe Resnick gave technical assistance for this study.

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TREATMENT OF HYPERTENSION WITH CHLOROTHIAZIDE

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After more than a year of clinical trials, chlorothiazide has become established as a valuable agent for the control of hypertension.[1] It is an especially important drug in general practice, because it can be administered according to straightforward dosage schedules and, in the presence of uncomplicated hypertension, has been relatively free of toxic reactions. Indeed, it has reduced the over-all incidence of toxicity and side-effects of antihypertensive drug therapy. When chlorothiazide is used, lower and, hence, less toxic dosages of other hypertensive agents, such as hydralazine or the ganglion blocking drugs, become effective in controlling blood pressure. The special circumstances under which toxicity can occur will be discussed later.

Mechanism of Effects

Previous reports from this laboratory[2] stressed the importance of salt loss in the mechanism of the antihypertensive effects of the drug. This view has been contested by Wilkins and co-workers.[3] However, further work in this laboratory in the interim has only strengthened the initial observations. These studies may be reviewed briefly here. When chlorothiazide was given to nonedematous, hypertensive

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When chlorothiazide is used, lower and, hence, less toxic dosages of other hypertensive agents become effective in controlling blood pressure. Chlorothiazide does not reduce blood pressure in normotensive subjects, although the drug induces the same increase in salt excretion. Regarding the mechanism of antihypertensive effect of chlorothiazide, it may be tentatively concluded that the blood pressure reduction accompanies the salt loss and probably is a consequence of it. When chlorothiazide is added to the regimen of a patient taking ganglionic blocking agents, the dosage of the latter must be reduced by half. The responsiveness of the patient is so remarkably increased by chlorothiazide that, if full dosage is continued, severe hypotension, including postural collapse, usually will occur. The other so-called toxic reactions to chlorothiazide are only extensions of its fundamental saluretic and kaluretic actions. Hypopotassemia is frequent, and potassium supplements should be used when this develops.

patients, a urinary loss of approximately 250 mEq. or roughly 1.5 Gm. of salt occurred primarily in the first 24 to 48 hours after the drug was administered. This depletion seemed to be derived in large measure from the extracellular fluid, since measurements of this space disclosed reductions of 1 to 2 liters. Accompanying the diminution in extracellular fluid space was also a reduction in plasma volume (fig. 1). The reduction in plasma volume had also been observed by Tapia and associates.[4] At the same time that these events occurred, the blood pressure fell. It did not precede the saluresis (urinary loss of salt) or follow days later.

These changes were not peculiar to chlorothiazide. They occurred also with ammonium chloride plus mercurials. It is as if well-compensated individuals are, in effect, slightly edematous. At least there seems to be an easily mobilized pool of extracellular fluid which can be skimmed off by saluretic drugs. Another point that leads one to believe that the antihypertensive effect of such agents is secondary to the salt loss is that if sufficient salt is given (and this may require as much as 25 Gm. per day) the antihypertensive effect of the drug is at least partially overcome.

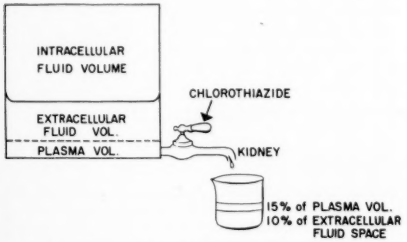

Fig. 1.—Effect of chlorothiazide in nonedematous patients.

Interestingly enough, chlorothiazide does not reduce blood pressure in normotensive subjects, although the drug induces the same increase in salt excretion. However, Dr. A. Wanko, in this laboratory, has shown recently that it changes vascular responsiveness in normal persons even though basal blood pressure is not altered.[5] The pressor response to arterenol is decreased, and the depressor response to ganglionic blocking agents is increased. Most important of all, the vascular responsiveness reverts back to pre-chlorothiazide-therapy levels when the plasma volume is restored with 500 ml. of a 6% solution of dextran.

Dr. I. M. Wilson, also in this laboratory, has carried out repeated determinations of plasma volume and extracellular fluid space in hypertensive patients treated for long periods.[6] She finds that some reduction persists until the drug is withdrawn, after which the volumes rise promptly to pretreatment levels.

At present, therefore, regarding the mechanism of antihypertensive effect of chlorothiazide, it may be tentatively concluded that (1) it has no unique hypotensive properties not shared by other saluretic agents, such as the mercurials; (2) the blood pressure reduction accompanies the salt loss and probably is a consequence of it; (3) the salt loss comes primarily from the extracellular fluid, and the drug produces a sustained reduction of extracellular fluid space and plasma volume; and (4) the reduction of plasma volume and of tissue pressure due to the extracellular fluid loss may play a role in reducing the basal blood pressure of hypertensive but not of normotensive persons and of vascular reactivity in both.

Combined Therapy

It is this increased responsiveness to depressor stimuli that makes chlorothiazide an effective agent in the management of hypertensive patients. By itself, it has only a moderate effect on blood pressure in most patients. But when any type of antihypertensive agent is given in conjunction with chlorothiazide, it gains a new depressor effectiveness. This is particularly true in the case of the ganglionic blocking drugs and of hydralazine (Apresoline) hydrochloride. Because dosages need be less, treatment becomes not only more effective but also simpler, since it is no longer necessary to skirt on the edge of toxic dose levels.

In order for maximum benefit to be obtained from chlorothiazide it must be remembered that hypertensive patients differ in their responsiveness to antihypertensive medicaments. For example, in a random group of 100 hypertensive patients, 20 of those with milder degrees may respond satisfactorily to chlorothiazide alone, 20 others to chlorothiazide and Rauwolfia preparations, and 40 to chlorothiazide and hydralazine, while the final 20 may require the ganglionic blocking drugs, at least for a time. Which of these combinations approaches most closely the ideal of general effectiveness, safety, tolerability, and simplicity? Experience here would indicate that in all forms of mild and moderate hypertension which merit any treatment at all the nearest approach to the ideal is represented by chlorothiazide and hydralazine.

The dosage of chlorothiazide in patients with hypertension uncomplicated by cardiac or renal failure can safely be 500 mg. given twice daily on arising and at bedtime. This will be an effective saluretic dosage in practically all patients, and it avoids the needless complications of titration. In this clinic, patients with uncomplicated hypertension have been given this dosage continuously for

more than one year without toxic effects. To this is added 25 mg. of hydralazine two or three times daily. If this dosage is insufficient, it is raised to 50 mg. three times daily but not beyond this level, since toxic effects can occur at higher dosages. Unlike some other antihypertensive drugs, this combination does not produce easy fatigue, lethargy, or mental dulling. One avoids the considerable danger of precipitating an emotional depression in intellectual persons who are given Rauwolfia, as well as the inconvenience of dosage juggling so frequently required with the ganglionic blocking drugs. Of course Rauwolfia, the ganglionic blocking agents, or both are added whenever the chlorothiazide-hydralazine regimen is ineffective. Dosage readjustments of the blocking drugs are not as frequently required in patients who are also taking chlorothiazide. In addition, the side-effects of ganglionic blockade are far less, due to the lower dosage requirement.

Toxic Reactions

It is necessary at this point to emphasize that, when chlorothiazide is added to the regimen of a patient taking ganglionic blocking agents, the dosage of the latter must be reduced by half. The responsiveness of the patient is so remarkably increased by chlorothiazide that, if full dosage is continued, severe hypotension, including postural collapse, usually will occur. For the same reason, care must be used in administering chlorothiazide to a patient who has previously undergone sympathectomy. This usually is well tolerated, but if such a patient is elderly or has arteriosclerosis there is the possibility of precipitating a coronary or cerebrovascular occlusion if the hypotensive response is marked.

The example just cited could be called a "toxic effect" of chlorothiazide, since the net result is deleterious to the patient. But in a more real sense it is not a failing of the drug, whose purpose is to lower blood pressure, so much as it is a reflection on physicians who proceed thoughtlessly in a situation where wisdom cautions otherwise. The blame in this case is not with the drug but with the physician's judgment.

Similarly, the other so-called toxic reactions to chlorothiazide hold no surprises but are only extensions of its fundamental saluretic and kaluretic actions (fig. 2). The most common of all the "toxic reactions" is hypopotassemia. In patients with uncomplicated hypertension, reductions of serum potassium levels to 3 mEq. per liter is almost commonplace and, in experience at this laboratory, has not been attended by clinical manifestations of hypokalemia or by any evidences of renal damage. The situation in a cardiac patient, on the other hand, has been quite different. Patients with resistant congestive heart failure appear to be potassium "losers," and the addition of chlorothiazide may tip the scale toward critical depletion. This clinical situation is further embarrassed by the fact that digitalis toxicity develops so readily in the presence of hypopotassemia. The first sign of trouble then may be the arrhythmias of digitalis intoxication.

Various measures may be taken to cope with this toxic development. The dosage of digitalis may be reduced or omitted, chlorothiazide may be given intermittently rather than continuously, or potassium supplements may be administered. I do not share the equanimity of other workers regarding the effectiveness of potassium supplements, since they may provide a false sense of security. Chlorothiazide is quite effective in removing excessive sodium in the diet and may do the same with potassium supplements. How much potassium is enough to raise the blood potassium level, and what happens when the patient forgets to take his supplement? These important questions need to be resolved, and it would seem advisable to supply an ample excess of 75 to 100 mEq. orally per day in all patients who develop hypokalemia. There is

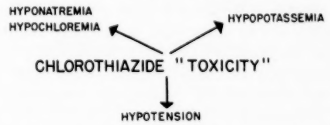

Fig. 2.—Reactions to chlorothiazide as extensions of its fundamental actions.

some evidence to suggest that the hypokalemia may be due to a secondary stimulation of aldosterone secretion.

In the patient who has congestive heart failure secondary to hypertension, it is usually possible to control the failure without digitalis after the blood pressure has been reduced and reaccumulation of edema prevented by chlorothiazide plus other hypotensive agents. There is no need to make a fetish of digitalis if it is harmful in a particular situation. A cautious trial of withdrawal after compensation has been restored will not subject the patient to any significant risk.

In the patient with congestive heart failure due primarily or completely to causes other than hypertension, it is our practice to continue digitalis therapy but to administer chlorothiazide intermittently (usually two days on treatment and two days off), thereby permitting nature to make its own compensations. Unfortunately, in patients with hypertension chlorothiazide must be taken daily, as the blood pressure rises promptly (within 24 to 48 hours) after the drug has been withdrawn.

By the same token, the physician should resist the temptation to give chlorothiazide for correction of hypertension or edema secondary to hyperadrenocorticism, either the naturally occurring varieties or the type induced by steroid treatment. The adrenal cortical hormones conserve sodium and waste potassium. Chlorothiazide increases the excretion of both. In the patient with potassium depletion and hyperadrenocorticism, the additional insult of chlorothiazide may precipitate severe hypokalemia. Similarly, protracted diarrhea, various renal tubular disorders, and ureterosigmoidostomy may in themselves produce potassium depletion and hence make chlorothiazide therapy dangerous. Fortunately, these are situations that rarely arise in the routine management of hypertensive patients.

It is surprising that hyponatremia and hypochloremia do not develop more frequently. There seem to be few authenticated cases, and these conditions have not been observed in this clinic. Once the labile pool of extracellular fluid has been skimmed off, chlorothiazide seems to become relatively ineffective in removing further sodium or chloride. Nevertheless, it would be adding insult to injury to give chlorothiazide in the presence of nephritis with salt loss, or of depletion of body stores of sodium or chloride, as can occur with protracted vomiting or severe diarrhea. On the other hand, last year patients treated with chlorothiazide at this clinic lived through the usual hot Washington summer without any evidences of salt deficiency.

One further word is required on the subject of "toxic reactions" to chlorothiazide. As organic renal damage progresses, the kidney vasculature loses its flexibility in adjusting to a reduced level of blood pressure. When blood pressure falls, glomerular filtration decreases. In the patients with elastic renal blood vessels, adjustments are made quickly so that filtration pressure is restored. But in the rigid vasculature of the patient with far-advanced nephrosclerosis or nephritis, these adjustments are poorly made, with the result that filtration pressure and filtration rate become lower and remain reduced. Such kidneys can ill afford this insult, since they depend on a high urine volume to hold uremia in check. As the filtration rate falls, oliguria develops and nitrogenous products accumulate in the blood.

In the presence of such renal damage and a high level of blood pressure, the physician truly must steer carefully between Scylla and Charybdis. If he aims toward hypotension, he must be aware of the possibility of uremia. But if he withholds therapy, his patient may be drawn further toward malignant hypertension. The only solution then is to proceed cautiously but firmly in the direction of moderating the level of blood pressure, watching scrupulously for oliguria, lightening treatment when this occurs, but pressing forward again watchfully when the danger has passed. Thus, judiciously the physician directs his course altering direction from time to time as prevailing conditions dictate. Few of these patients will be saved even under these circumstances. But the few who are makes the effort worthwhile.

Very often the level of blood urea nitrogen or nonprotein nitrogen will gradually rise. Even in these circumstances, I have persisted for a time, at least, hoping for the occasional instance in which the levels will stabilize and then gradually recede as the patient adjusts to the lower level of blood pressure.

Conclusions

The various complications to chlorothiazide therapy are not common in general practice, but awareness will aid in their prevention. Actually, the good produced by chlorothiazide far outweighs its harm. The discovery of this agent represents a therapeutic advance of considerable significance. The patient with uncomplicated hypertension who does not have congestive heart failure, renal failure, or steroid-induced hypertension has little to fear and much to gain from the use of this drug.

The goal of complete control of elevated blood pressure grows ever nearer. Will this prevent the organic complications that produce morbidity and mortality? I believe it will, but only time and thoughtfully planned studies will provide the final answer.

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CHLOROTHIAZIDE (DIURIL)—A NEW, NONMERCURIAL, ORALLY GIVEN DIURETIC

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and
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The diuretic effects of chlorothiazide were studied in four groups of patients with various degrees of congestive heart failure. All but 2 of the 50 patients were fully digitalized, and all were being kept on diets yielding 1 Gm. of sodium chloride per day. The usual dose for long-term therapy was found to be 250 or 500 mg. given thrice daily by mouth at roughly six-hour intervals for three or four consecutive days a week. Some individualization was necessary. Three case histories illustrate the gratifying results obtained in some patients; a fourth illustrates the fact that patients resistant to mercurial diuretics are generally resistant to chlorothiazide also. Under the conditions of this study, with the use of ammonium chloride and potassium chloride when indicated, no serious electrolyte imbalance occurred, and patients remained free from gastrointestinal and neurological symptoms of toxicity.

Clinical observation concerning a new, nonmercurial, orally given diuretic, designated by the generic name chlorothiazide,[1] constitutes this report. It is designated chemically as 6-chloro-7-sulfamyl-1, 2,4-benzothiadiazine-1,1-dioxide.

It is not primarily a carbonic anhydrase inhibitor [2] but seems to possess the factor of exerting considerable influence on the renal tubular transport of electrolytes, causing a marked decrease in the reabsorption of sodium and chloride and, to a lesser degree, potassium and bicarbonate.[3] The loss of sodium is apparently equal, mol for mol, to that of chloride.[3a] When given in large doses, it is reported [3a] that bicarbonate is lost in "appreciable" amounts, though never to the point of metabolic acidosis as in the case with carbonic anhydrase inhibitors. Smaller but effective diuretic doses produce only relatively minor loss of bicarbonate.

The drug is rapidly and well absorbed when given by the oral route, with onset of action within two hours and a duration of action of somewhat less than 12 hours.[4] The pattern of electrolyte excretion, with marked chloruretic effect and rapid onset, suggested a similarity to mercurial diuretics and, further, that pretreatment with ammonium chloride might enhance its effect and protect the patient from hypochloremic alkalosis.

Methods

Chlorothiazide (Diuril) was employed in several different groups of patients. All were kept on diets with 1 Gm. of sodium chloride, and all but two were fully digitalized. All other diuretic agents were withdrawn except ammonium chloride. There was a total of 50 patients in the study, which covered a period of seven months. All patients were in congestive failure at the time of drug administration. Since the completion of the study, an additional six months of use has occurred, making in all a 13-month period during which the drug has been employed.

Since chlorothiazide was reported [3] to cause a marked chloruresis, several patients were studied by a check of serum electrolyte disturbances. As the study progressed, routine determinations appeared unnecessary, since apparent protection against hypochloremia could be provided simply by ammonium chloride administration. The latter was given in 1-Gm. doses four times daily on three to four consecutive days per week, as with the mercurial diuretics. The substitution of enteric coated potassium chloride for ammonium chloride, 1 Gm. given three times daily for three days, may more completely protect the patients from chloride and potassium loss. The use of ammonium chloride, while it did protect the patient from hypochloremia and alkalosis, did not materially add any diuretic effectiveness and did not appear to enhance the effect of chlorothiazide. As of this time, we feel the use of enteric coated potassium chloride probably represents the drug of choice in place of ammonium chloride, as one can feel that chloride and potassium replacement will occur with a single medication.

Chlorothiazide was administered in divided doses ranging from 250 to 1,500 mg. per 24 hours, three to seven days a week. The average dose for long-term therapy was found to be 250 or 500 mg. given three times daily at roughly six-hour intervals. We observed that a greater diuretic response was obtained by giving chlorothiazide on a divided dosage schedule, two to three times a day, than by a single large dose in the morning and over three to four consecutive days each week. We observed that most patients could be kept at "dry" stable weights with three or four consecutive days of chlorothiazide administration; continuous daily administration did not seem necessary except in an occasional patient in whom control was more difficult.

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Read in the Symposium on the Newer Diuretics—Especially Chlorothiazide—Indications and Reported Use before the Section on General Practice at the 107th Annual Meeting of the American Medical Association, San Francisco, June 26, 1958.

Individual dosage adjustment was, of course, necessary, since all patients did not respond in a similar manner, some requiring as much as 1,500 mg. per day and others as little as 250 mg. one day a week. The usual initial dose was 250 mg. given three times a day for three or four consecutive days a week. Larger doses gave no greater diuresis than smaller effective doses, and we felt, further, that it was important to use the smallest possible effective dose for long-continued therapy. Subsequent dosage was determined by diuretic response and further need of therapy. There was no evidence of the loss of effectiveness of chlorothiazide in the presence of ammonium chloride acidosis.[5]

The onset of diuresis was more gradual than with a parenterally given mercurial agent, but continued in a more sustained and less vigorous manner, so that practically all patients agreed it did not cause them the same degree of muscular discomfort and marked frequency of urination, with the consequent frequent loss of sleep, seen with the shorter and more violent action of a parenterally given mercurial diuretic.

Results

Group 1 consisted of patients seen for the first time in congestive failure in whom chlorothiazide was administered in lieu of a mercurial diuretic. There were five patients in this group, three with arteriosclerotic heart disease, one with hypertensive cardiovascular disease, and one with rheumatic heart disease.

The average dosage of chlorothiazide was 250 mg. given three times a day for three days. The average weight loss was 6 lb. (2.7 kg.) at the end of a three-day period.

In group 2 were included patients in chronic congestive heart failure who required only occasional mercurial injections or were taking, orally, mercurial or nonmercurial diuretics. There were 25 patients, 9 with arteriosclerotic heart disease, 3 with hypertensive cardiovascular disease, and 13 with rheumatic heart disease.

Follow-up studies were done for periods of six weeks to four months, with an average of two and one-half months. The average dosage of chlorothiazide was 250 to 500 mg. given three times a day for three consecutive days each week. One patient received as little as 125-250 mg. one day a week. The average weight loss was 5 lb. (2.3 kg.). The usual loss was 3-8 lb. (1.3-3.6 kg.) at the end of each course.

No patient failed to be controlled as well as with mercurials given by oral or parenteral route or with orally given nonmercurials combined with mercurial agents. Three patients were improved much more than with the mercurial program. Two patients who had regularly received nonmercurial, orally given diuretics and, occasionally, mercaptomerin promptly lost 5-8 lb. when placed on chlorothiazide therapy. One patient who had been on therapy with an orally given mercurial agent lost 5 lb. in four days after use of chlorothiazide.

Group 3 included patients in chronic congestive heart failure who required regular injections of mercurial agents. There were 17 patients in this group, 11 with arteriosclerotic heart disease, 1 with hypertensive cardiovascular disease, and 5 with rheumatic heart disease.

Follow-up studies were done over periods of two to five months. The average dosage was 250 mg. given three times daily to 500 mg. given twice or three times daily for three consecutive days each week. Previous diuretic therapy had been with mercaptomerin alone or in combinations with chlormerodrin or nonmercurial, orally given diuretics. The average frequency of administration of mercurials by the parenteral route was every 7 to 14 days. After chlorothiazide therapy was begun, the average weight loss was 6 lb. and one patient lost 12 lb. (5.4 kg.).

No failures in treatment occurred. Every patient was as well controlled as, and a great deal more smoothly than, with the previous diuretic schedule.

In group 4 were patients in a refractory state of congestive failure in whom regular mercurials did not produce satisfactory results. There were three such patients, all with arteriosclerotic heart disease. All were unimproved on the mercurial program, and all were unimproved on chlorothiazide therapy. One patient noted some improvement after a return to mercurial therapy.

Report of Cases

Case 1 (group 1).—A 50-year-old man was admitted to the Henry Ford Hospital in congestive failure from arteriosclerotic and hypertensive heart disease. He had been on therapy with digitoxin, 0.2 mg. per day, and a low-salt diet. After admission, with no change in therapy, his weight remained stable for three days. On the morning of the fourth day, therapy with 500 mg. of chlorothiazide given twice daily was begun. At the end of two days, he had lost 7 lb. (3.2 kg.) in weight and all signs of congestive heart failure had cleared except for questionable minimal hepatic enlargement. He was continued on chlorothiazide therapy for three more days, with a further loss of 1 lb. (0.5 kg.) in weight. Serum sodium, potassium, chloride, and carbon dioxide levels were determined at this time, and all were within normal limits. He was then parenterally given 2 cc. of a mercurial to see if any further diuresis could be obtained. There was no change in weight or physical findings.

He was discharged to the outpatient department on maintenance therapy with digitoxin and a 1-Gm. salt diet, and follow-up examinations were done at about monthly intervals, with the requirement of parenterally given mercurials. After three months he showed evidence of increasing congestive failure. Chlorothiazide therapy was begun again, 250 mg. given three times daily three days a week, and ammonium chloride, 1 Gm. given four times daily the other four days of the week. Within 48 hours of institution of chlorothiazide therapy, he lost 4 lb. (1.8 kg.) in weight and his failure cleared. He has remained out of failure on this program for three months and has required no subsequent therapy with mercurial agents.

Case 2 (group 2).—A 44-year-old woman with rheumatic heart disease, auricular fibrillation, and chronic congestive failure had been on therapy with digitoxin, ammonium chloride, a 1-Gm. salt diet, chlormerodrin given five days a week, and, occasionally a parenterally given mercurial. When chlorothiazide therapy was begun, 250 mg. given three times a day three days a week, with 4 Gm. of ammonium chloride

the other four days of the week, she lost 5 lb. in weight within four days. Symptoms were relieved, and she has maintained her improvement for more than two months with no need for chlormerodrin or any parenterally given mercurial agent.

Case 3 (group 3).—A 70-year-old woman, treated at the Henry Ford Hospital for many years, had hypertensive cardiovascular disease, auricular fibrillation, and chronic congestive failure. She had been on therapy with gitalin, 0.5 mg. per day, a 1-Gm. salt diet, and rauwolfia (Raudixin), 100 mg. twice daily, and for many months had required parenteral injections of mercurial agents every 7-10 days with ammonium chloride given intermittently. Even on this program she had congestive failure periodically, with orthopnea, paroxysmal nocturnal dyspnea, and edema, usually beginning a few days prior to each injection of the mercurial. Chlorothiazide therapy was begun, 250 mg. given three times a day, three days a week and ammonium chloride the other four days of the week. On this program, she did not need any mercurial diuretic for five months and has had no orthopnea, paroxysmal nocturnal dyspnea, or edema for the first time in two or three years. It may be added that for 13 months the same continued satisfactory response has been seen.

Case 4 (group 4).—A 65-year-old man had chronic, severe, intractable congestive failure and auricular fibrillation on an arteriosclerotic basis. He had been on therapy with digitoxin, 0.625 mg. daily, a 1-Gm. salt diet, intermittently given ammonium chloride and parenterally given mercurials, and, in the past, chlormerodrin and acetazolamide. The condition had not been well controlled with any of these programs. Recently, he had become almost completely resistant to even parenterally given mercurials. Therapy was begun with 500 mg. of chlorothiazide given twice daily three days a week, with ammonium chloride given intermittently, without response. Dosage was increased finally to 500 mg. given three times a day every day, but still this produced no satisfactory response. To this program was added parenterally given mercurials, 2 cc. every three to seven days, but with only minimal improvement—that is, a weight loss of 3 to 4 lb. with each injection. However, he would regain this weight within 24 to 72 hours. In summary, it was felt that chlorothiazide was of no significant benefit to this patient.

Toxicity

Our studies to date indicate chlorothiazide has little or no toxicity; however, as with all new drugs, alertness for signs of toxicity must be maintained. Its greatest potential danger seems to be the possibility of producing hypochloremia, hypopotassemia, or low sodium level syndromes, exactly as with mercurials. No serious electrolyte imbalance occurred in this study.

Patients with kidney disease and those with liver function impairment should be watched closely. The drug is apparently primarily excreted by the kidney, being eliminated completely within 24 to 48 hours.[4] However, in dogs subjected to nephrectomy and given chlorothiazide, considerable quantities could be recovered from the biliary tract.[3a]

Nausea or vomiting did not occur in any of our patients, the drug being exceedingly well tolerated. No neurological symptoms, such as headache, paresthesias, or peripheral neuritis, were found. Skin eruptions were not encountered; hemorrhagic and renal disturbances were checked for but not present.[4] In short, no evidence of serious toxicity was discovered in any of the patients treated in this report. However, since the completion of the report, and in the additional six months of use of the drug, three cases of skin rash have been observed. One of these was a true morbilliform type of rash, similar to that seen with the use of sulfonamides. The other two were very fine macular rashes, erythematous in nature, promptly subsiding with discontinuance of therapy. In one case, the drug was readministered in a smaller dose without return of the rash. Since the drug is a compound related to the sulfonamides, this type of rash may be found in some patients. The exact incidence is not definitely known but probably is well under 2%.

We would like to state that it is advisable to respect the potential danger of this drug, as with the mercurials, in treatment of patients with salt depletion and to be cautious in using it without the replacement of chlorides and potassium by means of ammonium chloride or potassium chloride where the latter can be safely administered. In those cases in which sodium or potassium depletion may occur, as in serious liver disease or in the long-continued use of steroid therapy, hypopotassemia may occur earlier than is the usual case, since the cation of excretion with chlorothiazide is chiefly sodium and, where this is not present, the next available cation, potassium, will be excreted in fairly large quantities. In patients who are digitalized, this hypopotassemia may potentiate the digitalis effect, resulting in digitalis intoxication and its subsequent manifestations.

Comment

Chlorothiazide appears to represent a significant advance in the diuretic management of patients with congestive heart failure, approaching the effectiveness of parenterally administered mercurials; its decided advantages are (1) effective oral administration, (2) apparent lack of toxicity, (3) high patient acceptance, (4) sustained diuretic action over prolonged periods of use (months) without apparent development of tolerance to the drug, without necessity of increasing dosage, and, therefor, with more even control of failure than seen with intermittent parenterally administered mercurials, and (5) fairly rapid onset and peak of action.

Summary

Chlorothiazide (6-chloro-7-sulfamyl-1,2,4-benzothiadiazine-1,1-dioxide) was found to be an extremely effective, orally given, nonmercurial diuretic agent resembling most closely, pharmacologically, the mercurial diuretics. Therapeutic dosage varied from 250 to 1,500 mg. given daily with apparent increased effectiveness on a divided-dose schedule. The usual maintenance dose was 500 to 1,000 mg. given three to four consecutive days of each week, alternating with ammonium chloride for its antihypochloremic-alkalosis effect, or the concurrent use of postassium chloride, 600 mg. given four times daily to protect from hypochloremia and hypopotassemia.

Its effectiveness was not diminished with constant administration, even over a period of several months. Chlorothiazide was found to be an effective replacement for regular orally or parenterally given mercurial agents and resulted in a smoother control of failure than that seen with intermittently, parenterally given mercurials in the majority of cases. It was also effective in short-term diuretic action (one to three days). In our limited experience, it was of no value in intractable, mercurial-resistant cases.

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The chlorothiazide used in this study was supplied as Diuril by the Merck, Sharp & Dohme Research Laboratories, Division of Merck & Co., Inc., Philadelphia.

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CHLOROTHIAZIDE AND PREMENSTRUAL TENSION

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Diuretics have been used with some success in control of the premenstrual tension syndrome. This study shows that chlorothiazide is particularly useful in controlling the edema and breast swelling often associated with premenstrual tension and, to a lesser degree, the tension itself.

The premenstrual tension syndrome is composed of many symptoms, any or all of which may be found in an individual patient. Most women note some changes the week before their menses, usually insufficient to require medical attention. The principal complaints noted at that time are nervousness, tension, swelling, headaches, depression, and breast soreness and turgidity; in severe form, these symptoms may progress to antisocial behavior and psychosexual abnormalities. During the premenstruum, some women exhibit nymphomaniacal tendencies, while others may have complete revulsion for the sex act. They often engage in domestic quarrels and become so distracted and distraught that their work efficiency is considerably lessened. This condition is of great importance to industries in which large numbers of women are employed, since efficiency drops, use of sick leave increases, and worker productivity is decreased.

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The principal complaints of premenstrual tension noted a week prior to menses are nervousness, tension, swelling, headaches, depression, and breast soreness and turgidity; in severe form, these symptoms may progress to antisocial behavior and psychosexual abnormalities. Symptoms of the premenstrual tension syndrome may be due to latent edema, since many of the patients without apparent swelling were benefited by use of the diuretics alone. The usefulness of diuretics for control of premenstrual tension is well established. Chlorothiazide, in doses of 500 to 1,000 mg. administered daily for 7 to 10 days before menses, was given to 50 women with complaints referable to the premenstrual tension syndrome. Of the 50 patients, 33 complained of swelling. All of these patients showed an excellent response to chlorothiazide, with complete relief from their edema. Breast tenderness was a problem for eight patients, and, in each instance, the tenderness was relieved by chlorothiazide therapy. Headache was a presenting symptom in four patients, two of whom were relieved and two of whom noted no change while on chlorothiazide therapy.

The etiology of premenstrual tension is still not clear. Many theories have been advanced: menstrual toxins,[1] excessive circulating estrogens,[2] deficient progesterone production,[3] excessive antidiuretic hormone,[4] allergy to the ovarian hormones, hypoglycemia,[5] and vitamin B deficiency.[6] Since the symptoms are so variable in kind and intensity, the only major hypothesis which can explain the syndrome is a dysfunction of the hypothalamic control of the autonomic nervous system.[7] What might be responsible for this dysfunction remains to be solved.

Nevertheless, premenstrual tension is an important and ever-present complaint for which relief is sought. Many different types of medicaments have been advocated for this syndrome: B-complex vitamins to enhance estrogen metabolism by the liver, estrogens to prevent ovulation, progestational substances to supplement endogenous progesterone, sedatives to combat the nervousness, testosterone to antagonize endogenous estrogen, and diuretics to prevent excess salt and water retention, to name a few. All of these have their adherents and are helpful in some cases. At present, the most widely used agents for control of premenstrual tension are the diuretics.

The usefulness of diuretics for control of premenstrual tension is well established. When edema is apparent as one of the major symptoms during the premenstruum, diuretics, used for 7 to 10 days before the onset of menses, are effective in preventing fluid accumulation. In some patients, the edema may be latent in character and swelling not be obvious; in them, control of salt and water excretion may be accompanied by gratifying relief from the other symptoms of the syndrome.

Until recently, the available diuretics were of three main types: those that increased glomerular filtration, such as caffeine; those that increased tubular urea excretion, such as ammonium chloride; and those that decreased tubular reabsorption of water by inhibition of carbonic anhydrase, such as acetazolamide. Adequate response with caffeine and ammonium chloride requires administration at frequent intervals throughout the day, causing some inconvenience to the patient and often resulting in missed doses and, thus, decreased effectiveness. The carbonic anhydrase inhibitors become less effective after four to five days' continuous use, necessitating an interrupted schedule of administration for optimum effect. Coincident with interruption of the schedule, swelling may occur and symptoms become troublesome until the diuretic therapy can be resumed.

Since the newer diuretic, chlorothiazide, can be given continuously without the development of resistance, it has been tried for control of premenstrual tension in 50 women.

Results with Chlorothiazide

Chlorothiazide, in doses of 500 to 1,000 mg. administered daily for 7 to 10 days before menses, was given to 50 women with complaints referable to the premenstrual tension syndrome. To evaluate the effectiveness of this diuretic, the syndrome was broken down into four symptoms and the patients were judged on their relief from each symptom: nervousness and tension, swelling, breast soreness, and headaches (see table). An individual patient might have any or all of these symptoms.

Severe nervousness and tension was a symptom in 42 patients, of whom 21 had satisfactory relief with chlorothiazide alone. Addition of a mild sedative or tranquilizer, such as the barbiturate vinbarbital (Delvinal), meprobamate (Equanil), or promazine (Sparine) hydrochloride, usually alleviated this symptom in the patients in whom chlorothiazide alone was not satisfactory.

Of the 50 patients, 33 complained of swelling. All of these patients showed an excellent response to chlorothiazide, with complete relief from their edema. Breast tenderness was a problem for eight

Results of Chlorothiazide Administration in Fifty Patients with Premenstrual Tension

	Symptom							
	Tension		Swelling		Breast Soreness		Headache	
Daily Dose,* Mg.	Relieved, No.	Not Relieved, No.	Relieved, No.	Not Relieved, No.	Relieved, No.	Not Relieved, No.	Relieved, No.	Not Relieved, No.
500	6	11	12	0	4	0	0	0
1,000	15	10	21	0	4	0	2	2
Total	21	21	33	0	8	0	2	2

* Given 7-10 days before menses.

patients, and, in each instance, the tenderness was relieved by chlorothiazide therapy. Headache was a presenting symptom in four patients, two of whom were relieved and two of whom noted no change while on chlorothiazide therapy.

Comment

The premenstrual tension syndrome is of widespread importance, affecting most women to some extent. When it is sufficiently severe to require medical help, relief may be obtained from a great variety of therapeutic regimens.

Diuretics in some form have been used with moderate success for a long time in the treatment of this condition. Ammonium chloride, by increasing the urea excretion and altering the acidity of the urine, is one of the most popular diuretics and has met with variable degrees of success. With the advent of the newer diuretics, more uniform results have been obtained.

The major disadvantage of ammonium chloride is that its administration must be repeated at frequent intervals each day to attain an optimal re-

sponse, causing considerable inconvenience to the patient and often resulting in missed or irregularly spaced doses. Acetazolamide and other carbonic anhydrase inhibitors maintain their peak effectiveness for only four to five days, after which some swelling may occur. Chlorothiazide, on the other hand, continues to be effective for a prolonged period of time without the development of tolerance.

In the series of patients reported here who complained of premenstrual tension, chlorothiazide, given in a dosage of 500 to 1,000 mg. daily for the last 7-10 days before menses, was uniformly successful in preventing peripheral edema and breast tenderness. The nervousness and tension was relieved in one-half of these patients, whereas the balance of the patients noted no improvement. However, combining the chlorothiazide with a mild tranquilizer was effective in controlling the tension of those patients who noted no relief from chlorothiazide alone.

Premenstrual headaches were relieved in two of four patients with this complaint by chlorothiazide alone. The other two required the addition of tranquilizers.

This study supports the view that the symptoms of the premenstrual tension syndrome may be due to latent edema, since many of the patients without apparent swelling were benefited by use of the diuretics alone. On the other hand, it supports the contention that an alteration in salt and water metabolism is not the primary problem in all patients with premenstrual tension, since relief of all apparent swelling had no effect on the tension, nervousness, and headaches of half the patients with these complaints. This serves to reemphasize the fact that no single regimen of treatment is successful in all cases of premenstrual tension; treatment must be individualized to the presenting symptoms.

Summary

A newer, orally given diuretic, chlorothiazide, has been utilized in the treatment of 50 women complaining of premenstrual tension in a dose of 500 to 1,000 mg. daily for 7 to 10 days before menses. The effectiveness of its use was assessed by analysis of the relief of four major complaints referable to this condition, any or all of which may have been present in an individual patient.

Chlorothiazide is an excellent agent for relief of swelling and breast soreness associated with the premenstrual tension syndrome, since all patients with these complaints were completely relieved.

Where tension, nervousness, and headaches are major factors, chlorothiazide may provide relief; approximately half of the patients in this series were benefited, the others noting no improvement. Mild sedatives or tranquilizers given along with chlorothiazide were helpful in resistant cases.

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The chlorothiazide used in this study was supplied as Diuril through Dr. John R. Beem of Merck, Sharp & Dohme, Division of Merck & Co., Inc., Philadelphia.

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TREATMENT OF CANCER.—Advances in the treatment of cancer have been made in all the major fields of therapy, but critical assessment of the results obtained indicates that there is little justification for complacency. Although much has been achieved in affording the patient good palliation and enabling him to live in comfort with the disease, the long-term survival or "cure" rates have shown little improvement. Perhaps the most significant advance has been the clinician's appreciation that larger operations and more complex and powerful therapy machines do not, of necessity, confer better treatment on the patient. Assessment of the differing biological potentials of each individual cancer has led to a more careful selection of the appropriate form of treatment. Surgeon, radiotherapist, and chemotherapist are appreciating that the future of cancer therapy lies at the cellular or intracellular level and are directing their efforts and attention accordingly.—A. G. Jessiman, F.R.C.S., and F. D. Moore, M.D., Advances in the Treatment of Cancer, *The Practitioner*, October, 1958.

MORPHOLOGY AND RACIAL DISTRIBUTION OF FATAL COCCIDIOIDOMYCOSIS

REPORT OF A TEN-YEAR AUTOPSY SERIES IN AN ENDEMIC AREA

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The generalization that dark-skinned ethnic groups are particularly susceptible to infectious granulomas was tested in a study of 4,989 autopsies performed during a 10-year period in an area where coccidioidomycosis and tuberculosis were both constantly present. Difficulties were encountered in classifying the subjects as to race and also in settling diagnostic questions in cases of arrested or inactive granulomatous lesions, but in persons who died with coccidioidomycosis it was always easy to demonstrate the organisms in the lesions. Acute forms of coccidioidomycosis, with massive suppuration and overwhelming dissemination, occurred in Negroes, Caucasians, and Mexicans; so did the subacute or chronic meningitic forms without obvious visceral involvement. There was evidence that all three groups were living in unfavorable environments. Nevertheless the incidence of fatal disease showed some striking differences. The incidence of fatal coccidioidomycosis was only slightly higher in Mexicans than in Caucasians, but that in Negroes was 10 times as high as in Caucasians. The incidence of fatal tuberculosis was only slightly higher in Negroes than in Caucasians, but in Mexicans it was very much higher. A group of Filipinos living in particularly bad circumstances appeared to be particularly vulnerable to both diseases. The supposed generalization, therefore, did not hold, and it is evidently important to specify which ethnic group and which infectious granuloma is concerned.

The meticulous study of Forbus and Bestebreurtje [1] and the admirable review by Fiese [2] suggest the desirability of further data on the morbid anatomy and race-sex distribution of fatal coccidioidomycosis. Observations on the histopathology of coccidioidomycosis have been presented elsewhere.[3] In view of the increasing national interest in the disease, it seemed appropriate to analyze an experience with fatal cases studied at autopsy in a civilian hospital in an endemic area with reference to morphology and race distribution. Data on fatal tuberculosis in the same autopsy population are presented for comparison and contrast.

Methods and Material

The Kern County General Hospital has 500 beds for acutely and 200 for chronically indigent sick persons of the southernmost county of the San Joaquin Valley. It is affiliated with the county tuberculosis sanitarium in a neighboring community. Figures for admissions for six years (July, 1951, to July, 1957) total 63,015—26,125 male and 36,890 female. A great many of the latter were admitted to the obstetric service. The figures by race are as follows: Caucasian, 40,163; Mexican, 11,958; Negro, 10,142; and others, 752. The conclusion as to race was based on the individual's statement plus data on parents and their place of birth. Mexican, I believe, can be defined as a person with a Spanish name with some Spanish blood but largely American Indian (Amerind) parentage, whether born in California, Texas, Arizona, New Mexico, or old Mexico. Unfortunately, the census statistics list most Mexicans as Caucasian, despite the importance of the Amerind strain.

The pathology laboratory of the hospital was under the direction of Dr. J. D. Kirshbaum from late 1946 to early 1949 and has been supervised by myself since April, 1950. From Jan. 1, 1947, to Dec. 31, 1956, 4,989 postmortem examinations were done. About one-third of these were done by request of the coroner on persons who died outside the hospital. However, many of these subjects had prior county hospital records, and most of them belonged to the indigent rather than the affluent class. Supplementary data on the race of these subjects were obtained from the police and the coroner when necessary.

Of the 4,989 subjects in the series, 3,383 were males and 1,606 females. The preponderance of males reflects the generally observed higher male mortality. In this area there is, perhaps, an unusual number of unattached males who take very poor care of themselves. Thus, for example, the Filipino colony at the northern end of the county is almost entirely male. Caucasian subjects numbered 3,558 (2,471 male and 1,087 female); Mexican, 629 (369 male and 260 female); Negro, 667 (431 male and 236 female); Filipino, 58 (all male); and other or unidentified races, 77 (54 male and 23 female).

Autopsy procedure has included microscopic study of any gross lesions and routine sections of major viscera even in the absence of gross lesions. Hotchkiss-McManus and acid-fast stains and cultures on Sabouraud's and Petragnini's mediums have been utilized freely.

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In none of the persons who died from coccidioidomycosis was there difficulty in demonstrating the organisms in the lesions. In a few with tuberculosis, antibiotic treatment insufficient to arrest the disease interfered with the demonstration of Mycobacterium tuberculosis post mortem. However, in all listed as having fatal tuberculosis, M. tuberculosis was demonstrated some time during the course of the disease; usually, it was found abundantly in tissue, at postmortem examination.

With arrested or inactive granulomatous lesions, the differential etiological diagnosis is frequently impossible. A solitary inactive subpleural granuloma showing spherules on wet mount or on section stained with hematoxylin-eosin or Hotchkiss-McManus stains can confidently be classed as coccidioidal, even though such lesions have not yielded viable organisms on culture.[2] A lesion of similar appearance but showing M. tuberculosis on section, smear, or culture can be classed as tuberculous. However, a great many such lesions show neither fungi nor M. tuberculosis. No attempt has been made, therefore, to compile figures for nonfatal tuberculosis, while those for nonfatal coccidioidomycosis are presented with emphasis on their incompleteness.

Results

After careful review, 63 deaths were attributed to coccidioidomycosis. One was due to hemorrhage from a chronic cavity. A Negro woman who had refused surgery died at home. Cultures of sputum had shown coccidioides immitis, and postmortem cultures of tissue were likewise positive. Sections showed the organisms to be largely in the mycelian phase. Two deaths were due to acute suppurative coccidioidal pneumonitis without evident dissemination. In the remaining 60 patients the disease had spread beyond lungs, pleura, and thoracic lymph nodes, i. e., it was disseminated. Meningitis was demonstrated in 39 of these. However, it was the sole metapulmonary lesion in only 10. Twenty-nine showed meningitis plus visceral dissemination, and it may be well to emphasize that this, in my experience, has been the most common pattern of fatal coccidioidal disease. In 17 with fatal disseminated disease there was no meningitis and in 4 the meninges were not examined. Of the 60 subjects with disseminated disease, 8 had bulky psoas abscesses.

One important lesson was the fact that the antemortem diagnosis of fatal coccidioidomycosis is not infrequently missed, even in clinics in which a good deal of it is seen. Chronic coccidioidal meningitis and acute disseminated coccidioidomycosis with subcutaneous abscess or cutaneous granuloma are not often overlooked, but other forms may well be. Thus, the diagnosis was missed prior to autopsy in the two cases of acute pneumonitis without dissemination and in eight cases of disseminated disease. Coccidioidomycosis should, therefore, be suspected in any obscure febrile illness in a person who has been in an endemic area.

Of the 63 subjects, 11 were Caucasian male, 6 Caucasian female, 5 Mexican male, 23 Negro male, 12 Negro female, 4 Filipino male, and 2 other male (1 Chinese, 1 Amerind). Of the 17 subjects with disseminated disease without meningitis, who presumably died of the dissemination before they had time to get meningitis, 14 were Negro and 1 was Filipino. Of the eight with psoas abscess, one was a Caucasian male, one a Filipino, and the remainder Negroes (five male, one female). On the other hand, of the 10 with meningitis as the sole metapulmonary lesion, only 2 were Negro and 1 Filipino. Four were Caucasian. The data on fatal coccidioidomycosis are summarized in table 1.

TABLE 1.—*Incidence of Fatal Coccidioidomycosis in Autopsy Series, 1947-1956*

Population Group*	Meningitis, No.				Visceral Dissemination Without Meningitis, No.			Visceral Dissemination with Meningitis, Not Determined, No.	Fatal Dissemination, Total	Fatal Acute Pneumonitis, No.	Fatal Cavity, No.	Total Fatalities	
	Lung Only	Without Psoas Abscess	With Psoas Abscess	Total	With Psoas Abscess	Without Psoas Abscess	Total					No.	%
Caucasian													
Male (2,471)	2	7	...	9	...	...	...	1†	10	1	...	11	0.455
Female (1,087)	2	3	...	5	...	1	1	...	6	...	...	6	0.552
Mexican													
Male (369)	2	1	...	3	...	1	1	1	5	...	...	5	1.36
Negro													
Male (431)	1	7	2	10	3	8	11	2	23	...	...	23	5.34
Female (236)	1	5	1	7	...	3	3	...	10	1	1	12	5.08
Filipino													
Male (58)	1	1	1	3	...	1	1	...	4	...	...	4	6.90
Other													
Male (54)	1‡	1§	...	2	...	...	...	...	2	...	...	2	...
Total (4,989)	10	25	4	39	3	14	17	4†	60	2	1	63	1.26

* Numbers in parentheses refer to group totals from which fatality percentages are derived (there were 260 Mexican females and 23 "other" females without findings relating to coccidioidomycosis; there were no Filipino females in study).
† One with psoas abscess.
‡ Amerind.
§ Chinese.

Data on 71 cases in which nonfatal coccidioidomycosis could be diagnosed are given in table 2. As already mentioned, the true incidence of inactive pulmonary residuals is certainly much higher than these figures indicate. At present, no way is known to recognize such residuals as coccidioidal in the absence of stainable spherules. Some comment on the 10 cases listed as "nonfatal disseminated" may be appropriate. In two of these cases, the diagnosis had been established during life, but no definite traces of it could be found at autopsy. A middle-aged Negro woman had a retropharyngeal abscess which yielded C. immitis on culture. She died, three and one-half years after diagnosis, of a carcinoma of the cervix. At autopsy, a subpleural granuloma showed neither acid-fast bacilli nor spherules. No other possible or probable coccidioidal lesions could be found. A 1-year-old Mexican boy had pneumonitis in 1948, followed by numerous skin and bony abscesses full of C. immitis and

TABLE 2.—*Incidence of Nonfatal Coccidioidomycosis in Autopsy Series, 1947-1956*

Population Group*	Inactive Pulmonary Disease, No.	Pneumonitis, No.	Cavitation, No.	Dissemination, No.	Total No.	Total %
Caucasian						
Male (2,471)	23	2	1	5	31	1.25
Female (1,087)	13	...	1	...	14	1.29
Mexican						
Male (369)	...	1	...	1	2	0.542
Female (260)	2	...	...	...	2	0.769
Negro						
Male (431)	12	...	...	1	13	3.02
Female (236)	4	...	2	1	7	2.97
Filipino						
Male (58)	...	...	...	2	2	3.45
Total (4,989)	54	3	4	10	71	1.42

* Numbers in parentheses refer to group totals, from which disease total percentages are derived (there were 77 in the "Other" category without findings relating to nonfatal coccidioidomycosis; there were no Filipino females in study).

a high complement-fixation titer. With treatment with a drug now believed of little value the lesions dried up. He died of sympathoblastoma with widespread metastases in 1952, and no coccidioidal residuals could be found at autopsy. Clearly, therefore, a person who has serious coccidioidal disease will not necessarily die of it. In six patients the metapulmonary lesions were few and apparently inactive. In two subjects the process might well have proved fatal if something else had not intervened first. In one of these (a Filipino male) the actual cause of death appeared to be chronic glomerulonephritis, while in the other (a Caucasian male) it was coronary artery disease.

In this series of 4,989 autopsies, there are 99 cases in which, on review, death is attributed to tuberculosis (table 3). Unfortunately, many of these autopsies were not done with the enthusiastic thoroughness which characterized those done to determine coccidioidomycosis. Thus, in too many instances the meninges were not examined. The disease appeared restricted to the lungs in 30, while there was evidence of dissemination in 69. Twenty-nine of the subjects were Caucasian male, 12 Caucasian female, 18 Mexican male, 23 Mexican female, 11 Negro male, 2 Negro female, 3 Filipino male, and 1 Amerind male. The disease appeared local-

TABLE 3.—*Incidence of Fatal Tuberculosis in Autopsy Series, 1947-1956*

Population Group*	Location: Disseminated, No.	Location: Localized Pulmonary, No.	Total Fatalities: No.	Total Fatalities: %
Caucasian				
Male (2,471)	14	15	29	1.17
Female (1,087)	8	4	12	1.10
Mexican				
Male (369)	16	2	18	4.88
Female (260)	19	4	23	8.85
Negro				
Male (431)	6	5	11	2.55
Female (236)	2	...	2	0.849
Filipino				
Male (58)	3	...	3	5.17
Other				
Male (54)	1†	...	1	...
Total (4,989)	69	30	99	1.98

* Numbers in parentheses refer to group totals, from which fatality percentages are derived (there were 23 "Other" females without findings relating to coccidioidomycosis; there were no Filipino females in study).
† Amerind.

ized in 15 of the Caucasian males and 5 of the Negro males. Localized disease was relatively less frequent in the other groups.

Comparative racial incidence of fatal coccidioidomycosis and fatal tuberculosis is given in table 4. It will be noted that the Filipinos appear decidedly vulnerable to both diseases and that coccidioidal deaths were much more frequent than tuberculous

TABLE 4.—*Comparison, by Race, of Incidence of Fatal Coccidioidomycosis and Fatal Tuberculosis in Autopsy Series, 1947-1956*

Population Group	Total in Group	Fatal Coccidioidomycosis: No.	Fatal Coccidioidomycosis: %	Fatal Tuberculosis: No.	Fatal Tuberculosis: %	Ratio (%)
Caucasian						
Male	2,471	11	0.455	29	1.17	38.0
Female	1,087	6	0.552	12	1.01	50.0
Mexican						
Male	369	5	1.36	18	4.88	27.8
Female	260	...	...	23	8.85	...
Negro						
Male	431	23	5.34	11	2.55	209.0
Female	236	12	5.08	2	0.849	600.0
Filipino						
Male	58	4	6.90	3	5.17	133.0
Other (male)	54	2*	3.70	1†	1.85	...
Series Total	4,989	63	1.26	99	1.98	63.6

* 1 Amerind; 1 Chinese.
† Amerind.

deaths in the Negroes, while tuberculous deaths were the more numerous in the Caucasians and the Mexicans.

Comment

Under the leadership of Drs. Claude Babcock, Bert Cotton, Ralph Cunningham, George Paulsen, and others, this community has kept pace with

modern methods for detection and medical and surgical treatment of tuberculosis. The county is rightly considered a hyperendemic area for coccidioidomycosis. It is of some interest, therefore, that in this autopsy series the fatalities due to tuberculosis exceeded those due to coccidioidomycosis. There was definitely less enthusiasm in requesting consent for autopsy in cases of known tuberculosis than in those of known coccidioidomycosis. Probably, therefore, the actual difference in fatality between the two diseases is even greater than these figures indicate.

The apparent vulnerability of the small Filipino group to both diseases may perhaps be attributed in part to their exceedingly unfavorable environment. However, it is doubtful whether the Caucasian, Mexican, and Negro populations represented in this autopsy series differ markedly in nutrition, domestic crowding, and exposure to agricultural dust. The differences in incidence of fatal coccidioidomycosis and fatal tuberculosis, and in the ratio between the two, among these three groups are, therefore, of considerable interest.

It will be noted that the incidence of fatal tuberculosis among the Negro females was of the same order as that among Caucasian males and females, while the incidence among Negro males was a little higher. The difference in incidence between Negro males and Caucasian males is slightly less than twice its standard deviation and, hence, probably not significant. The difference between the total Caucasian and Negro fatal tuberculosis rate is likewise between 1 and 2σ. Since larger statistical surveys [4] from other areas have established a significantly higher tuberculosis death rate in Negroes than in Caucasians, these figures may reflect merely the smallness of the samples and the decidedly underprivileged status of the Caucasian group. However, the incidence of fatal coccidioidomycosis in Negroes in this series appears about 10 times that of Caucasians; these differences are outstandingly significant. Conversely, the difference in incidence of fatal coccidioidomycosis between Caucasian and Mexican males is probably not significant, while the difference between all Caucasians and all Mexicans in this respect is less than 1σ. Yet, there is four times as much fatal tuberculosis in Mexican as in Caucasian males and eight times as much in Mexican as in Caucasian females, and, here again, the differences are statistically significant. Current figures on admissions to the county tuberculosis sanitarium corroborate the belief that in this area tuberculosis is conspicuously a Mexican disease. Finally, direct comparison between the Negro and Mexican groups, small though the numbers are, shows fatal tuberculosis to be significantly more common in the Mexicans and fatal coccidioidomycosis significantly more common in the Negroes.

With regard to the types of fatal coccidioidal disease seen in Caucasians, Mexicans, and Negroes, it will be noted (table 1) that, while massive suppuration, as represented by psoas abscess, and overwhelming dissemination ending fatally before meningitis can develop both occur in all three races, they are more common in the Negro than in the Caucasian or Mexican. Conversely, subacute or chronic meningitis without obvious visceral dissemination was noted twice in Negroes, twice in Mexicans, and four times in Caucasians.

It is suggested, therefore, that generalizations such as "the dark-skinned races are particularly susceptible to infectious granulomas" may be of very limited usefulness. At least in speaking of Mexicans and Negroes, in regard to coccidioidomycosis and tuberculosis, it seems important to specify which race and which infectious granuloma.

Summary

In a study of a 10-year autopsy series, comprising 4,989 autopsies, in a hyperendemic area of coccidioidomycosis, there were 99 fatalities attributable to tuberculosis as compared with 63 to coccidioidomycosis. The incidence of fatal tuberculosis was only slightly higher in Negro subjects than in Caucasian, but the incidence of fatal coccidioidomycosis in the Negroes was about 10 times that in Caucasians. Conversely, the incidence for Mexicans of fatal coccidioidomycosis was only slightly higher than that of the Caucasians, while that of fatal tuberculosis was very much higher. Filipinos appeared particularly vulnerable to both diseases. Fulminating dissemination of coccidioidomycosis and massive suppuration, although it occurred in Caucasians and Mexicans, was much commoner among Negroes.

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SYMPTOMATIC HIATUS HERNIA

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Herniations through the esophageal hiatus of the diaphragm often give rise to elusive symptoms that are common to many other abdominal disorders; they sometimes also lead to peptic esophagitis, severe hemorrhages, and strictures. The authors recommend that medical management be tried first but that operation be performed if such management fails to relieve symptoms. Of 65 patients who underwent surgery for symptomatic hiatus hernia, 45 had complained of pain that was poorly localized but commonly described as a sensation of fulness, bloating, or pressure. Esophagoscopy was carried out in 48 patients, and the findings were reported normal in 22. Surgical repair can be done by either the thoracic or the abdominal route. The essential aim is to bring the gastroesophageal junction back into position below the diaphragm and to keep it there. The hernial sac must be destroyed without injury to the sphincteral mechanism about the cardia. This depends upon a thorough understanding of the functions of the crura of the diaphragm, the muscularis mucosae and muscularis externa of the stomach, various parts of the endoabdominal fascia, and the left gastric artery in maintaining the usual position of the cardia. Close attention to detail is mandatory. The patients of this series were followed for periods of time from six months to seven years, and 59 of the 65 became and remained free from symptoms after operation.

Most patients with symptomatic hiatus hernia can exist indefinitely on a medical regimen if the physician and patient are satisfied with a chronic state of semi-invalidism.[1] After moderate symptoms have become established, it is rare that cure will result without surgical treatment. Herniation of the cardia through the hiatus causes loss of integrity of the cardioesophageal valve, allowing reflux of gastric juice into the lower part of the esophagus. The repeated insults of the acid-pepsin with resultant escharotic action cause permanent damage and eventual destruction of the enigmatic one-way valve. Medical treatment may suppress the symptoms by neutralizing gastric acid; however, the treatment schedule must be rigidly followed. Many patients will not adhere to a strict program, and the peptic esophagitis progresses. The vulnerable mucous membrane and muscularis mucosae of the lower part of the esophagus are eventually destroyed, resulting in stricture with chronic dysphagia, pyrosis, and malnutrition.

The increasing awareness of hiatus hernia as a cause for bizarre and elusive symptoms is interesting, with the number of operations performed for this disease increasing markedly in recent years. Analysis by year for this hospital reveals 9 operations in 1950, 3 in 1951, 2 in 1952, 5 in 1953, 5 in 1954, 17 in 1955, 11 in 1956, and 13 in 1957 (total, 65). It is still curious, however, to note how many doctors refuse to accept hiatus hernia as a cause for symptoms. The skeptics would soon revise their opinions if they had under their care miserable patients with esophageal strictures secondary to the peptic esophagitis of hiatus hernia.

Materials

This is a report of 71 patients who received surgical treatment for symptomatic diaphragmatic hernia at the Wadsworth General Hospital between 1950 and 1957. Types of hernia included sliding (61), paraesophageal (4), traumatic (4), pleuroperitoneal (1), and congenital short esophagus (1). The youngest patient was 23 years old and the oldest 72 years, with a mean of 55.6 years. Of the 65 patients with symptomatic hiatus hernia, 22 were in the 50-to-59 age group, 25 in the 60-to-69 group, and 4 over 70 years of age. Fourteen patients were below 50 years of age, with 2 in the 20-to-29 group, 3 in the 30-to-39 group, and 9 in the 40-to-49 group.

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Diagnosis

The symptoms are not specific and are common to many disorders of the upper part of the abdomen and angina pectoris. Pain was the most constant symptom, occurring in 45 (68.2%) cases, and consisted of a sensation of fulness, bloating, pain radiating to back, postprandial recumbency pain usually in the epigastrium, and pressure symptoms. Pyrosis and vomiting each occurred 25 (37.9%) times, and dysphagia occurred in 22 (33.3%) cases. Bleeding occurred in 21 (32.3%); in nine patients the bleeding was severe, and one required four transfusions in another hospital. It would have been

our practice to repair this hernia as soon as the patient had had adequate blood replacement. This patient eventually required an operation.

In 51 patients the duration of symptoms was less than six years, and in 28 of these it was less than two years. The remaining 15 had symptoms ranging up to 32 years' duration.

In all but one patient the diagnosis was established preoperatively by roentgenograms. In this one patient the hernia was discovered incidentally during a gastrectomy for ulcer disease and was repaired concomitantly.

Esophagoscopy was performed in only 48 cases, but it is now our firm belief that all patients with symptomatic hiatus hernia should have esophagoscopy performed prior to surgery. Esophagoscopic examination will enable the surgeon to accurately evaluate the lower part of the esophagus for evidence of esophagitis, ulceration, and stricture. Severe inflammatory changes may persist for prolonged periods after surgery, and in some cases the patient will have delayed too long in seeking aid and irreversible changes will have taken place.

Findings in 48 patients (72.7% of the total group) who had esophagoscopy were as follows: In 22 (45.8%) results were reported as normal. Twenty-one (43.8%) had esophagitis, three (14.3%) with ulceration, two (9.5%) with stricture, and one (4.8%) with associated ulceration and stricture. Esophageal stricture with normal mucosa above it was present in three patients (6.3%). The latter represents nature's attempt to protect the mucosa above the level of the stenosis from the corrosive action of gastric juices, but it does not improve the comfort and nutrition of the patient. Congenital short esophagus was reported on two occasions (4.2%); however, at surgery only one of these proved to be a true congenital lesion, the other representing a high cardioesophageal junction from recoil elastic shortening of the esophagus.

In addition to evaluating esophagitis, esophagoscopy is of value in eliminating the presence of a neoplasm in the hernia not diagnosed by the x-ray studies. We have not seen malignant tumors associated with hiatus hernias; however, Robb [2] reported three cases, and Grimes and Stephens [3] two. The combination of hiatus hernia and malignant tumor is admittedly rare, but knowledge of its existence prior to surgery would minimize the importance of the hernia in favor of the neoplasm and thus change the operation performed.

Associated diseases in the upper part of the abdomen and angina may be misleading, and in many patients errors in diagnosis have been made prior to discovery of the true cause of symptoms. Harrington [4] states that an average of three erroneous diagnoses were made in each of his cases; he lists them as cholecystitis, peptic ulcer, hyperacidity, secondary anemia, heart disease, carcinoma of the cardia, stricture, intestinal obstruction, appendicitis, and thoracic tumor. We have encountered similar situations, and where two diseases occur simultaneously the problem of distinguishing which disease is causing the symptoms sometimes presents a problem. We have used diagnostic pneumoperitoneum [5] a few times to help identify the symptomatic process and are encouraged by its results in difficult diagnostic problems. Induction of pneumoperitoneum apparently causes reduction of the hernia when the patient is in the upright position, and if symptoms are due to the hernia they will be relieved. When the patient is in the supine position, herniation again occurs and symptoms reappear.

Of the 65 patients 21 (32.3%) had peptic ulcers, and we feel there is a strong association between these two conditions, with the common denominator being gastric hyperacidity. Of the 21 patients who had esophagitis, 12 also had gastric or duodenal ulcer. It is now our custom to obtain studies for gastric acidity, and in many this level is high.

Burford and Lischer [6] advised use of Finney pyloroplasty alone in treatment of hiatus hernia with simple esophagitis, the concept being that pyloroplasty assures downward outflow of gastric acid pepsin, thus preventing reflux by decreasing resistance at the pylorus. With high gastric acidity or with peptic ulcer, associated with hiatus hernia, a more satisfactory procedure would be repair of the hernia and performance of vagotomy and pyloroplasty.

Esophageal acid reflux studies and Bernstein's test [7] are helpful in difficult problems. In the latter test, a small plastic tube is passed into the distal part of the esophagus and either dilute hydrochloric acid or saline solution is dripped through the tube. When esophagitis is present, the dilute acid will cause reduplication of the symptoms as it reaches the distal part of the esophagus but the saline solution will not. This test is more accurate in assessing mild degrees of esophagitis than is esophagoscopy, since the earliest changes are submucosal and not mucosal and, therefore, not visible to the naked eye.

Previous Treatment

Forty-three patients had received nonsurgical treatment, and 24 (48%) had been under apparently adequate medical management for a period ranging from several months to 11 years. The evaluation of prior medical treatment from the patient's history is sometimes difficult, but under adequate treatment we included those who stated they had been under prolonged care directed by a physician, clinic, or hospital. It should again be emphasized that many persons will not follow the ideal treatment program so necessary to control the regurgitant esophagitis. Seven patients (14%) had had one or more previous operations directed at repair of the hernia; they represented a special challenge,

since such hernias have a higher recurrence rate than those in patients not previously operated on. Sixteen (24.2%) had received no prior treatment.

Operation

Most of the operations were performed by residents in general and thoracic surgery, with variations in technique being utilized. The basic principles of repair can be accomplished through either abdomen or chest, and these principles should not be compromised, whichever route is used. When associated abdominal disease is present the abdominal approach may be preferable, in that treatment of both lesions can be done simultaneously. In some patients exposure through the abdomen is so difficult that it becomes a tedious and almost impossible operation. The transthoracic approach, in our hands, has been more satisfactory, and even the cases which would appear most trying are reduced to technically easy operations. The periesophageal inflammatory adhesions and fibrosis can be properly managed under direct view through the chest approach.

The most important factor in repair of hiatus hernia is to reduce the gastroesophageal junction below the diaphragm and maintain it there. If the phrenoesophageal ligament is of sufficient strength, it should be sutured to the abdominal surface of the diaphragm; however, frequently this ligament is a tenuous, almost ethereal membrane of little value. The crura should be approximated posteriorly, since anterior approximation changes the normal relationships between the esophagus and the crus, with backward displacement from its normal position, and leaves open the weak, unprotected area posteriorly. The hernia sac must be destroyed and the pinchcock mechanism kept intact by avoidance of injury to the cardia, crura, and oblique angle of the esophageal entrance into the stomach.

Results

Of the 65 patients who were operated on, 59 (90.8%) have been asymptomatic over a follow-up period ranging from six months to seven years. This compares favorably with other reported series.[3] In five (7.7%) results are classified as failures because of persistent symptoms; however, three of these patients complain only of "gas." One has a recurrent stricture, and one had severe esophagitis when last seen.

One patient died on the fourth postoperative day of a massive pulmonary atelectasis, and autopsy revealed an unrecognized, clear-cell carcinoma of the kidney and cirrhosis of the liver. This one death represents a mortality of 1.5%.

There were five (7.7%) complications of surgery, one of which was a nosocomial staphylococcic pericarditis which has cleared on antibiotic treatment (10-month follow-up). One patient had postoperative partial gastric volvulus with pyloric obstruction and recovered after a subtotal gastrectomy was done. Two have chest wall pain which is severe and persistent, and one had persistent esophageal stenosis eventually treated by esophagogastrectomy. Of the patients with complications, none have, at the time of writing, hiatus hernia symptoms and in two the complications cleared with further treatment.

Forty-four (67.7%) of the 65 patients were studied postoperatively with x-rays, and 7 (10.8%) had a small recurrence of the hernia. All but one were asymptomatic, and in this one case symptoms were controlled by medical management.

Comment

The gullet traverses the posterior mediastinum from the hypopharynx to the abdomen and passes through the hiatus. Its normal elastic recoil action pulls it upward against the forces which tend to maintain the normal anatomic relationships. The right and left diaphragmatic crura arise from the bodies of the first three or four lumbar vertebrae. The left fans out onto the diaphragm and does not contribute to the hiatus. The hiatus (fig. 1A) is formed entirely from the right crus as a teardrop-shaped split in the muscle fibers.[8] The right crus originates on the vertebral bodies, arcs up anteriorly along the gentle curvature of the diaphragm, passes around the esophagus to the left, and passes downward posteriorly toward the right where it meets its ascending limb. In the posterior area behind the esophagogastric junction is a fat pad which is unsupported and unprotected. In the supradiaphragmatic region this represents the posterior mediastinum, and the herniated stomach passes in this direction and upward. Herniation of the bare area

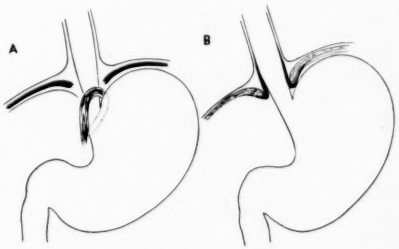

Fig. 1.—*A*, hiatus shown from anterior aspect illustrating formation of hiatus by right crus of diaphragm. *B*, phrenoesophageal ligament shown from anterior aspect. Heavy black lines illustrate ligament as continuation of endoabdominal fascia up through hiatus and insertion onto esophagus.

of the stomach and esophagogastric junction is comparable to a sliding hernia of the sigmoid colon, and reduction at surgery is accomplished in the same manner.

The endoabdominal fascia is a continuum and, in different areas, bears different names. In the lower part of the abdomen it is called the transversalis fascia; however, at the diaphragmatic hiatus region it is called the diaphragmatoesophageal fascia or phrenoesophageal ligament.[9] It ascends through the hiatus and, 1 or 2 cm. above the esophagogastric junction, inserts onto the esophagus and helps maintain the normal relationship of the esophagogastric junction to the diaphragm (fig. 1*B*). The peritoneum is loose and is generally not considered to have any effect in this regard. The ligament is resilient and allows considerable play of the esophagus through the hiatus.

According to Barrett,[10] the left gastric artery plays the most important role in maintaining the usual position. It tethers the upper lesser curvature aspect of the stomach to the posterior abdominal wall and helps resist herniation; however, if stretched it will allow the cardia to slip into the mediastinum.

The intrinsic muscular sling of the stomach is a band of gastric muscularis which passes from the lesser curvature posteriorly around the esophagogastric junction to the anterior aspect of the stomach and assists the hiatal sling in maintaining the acute oblique angle of entrance of the esophagus into the right side of the stomach.[10] Loss of the acute angle, such as with depression of the fundus of the stomach by the tonic contraction of the diaphragm during vomiting, causes incompetence of the cardia.

The exact mechanism of action of the one-way valve is not known; however, the oblique angle of entrance of the esophagus into the stomach is felt to be very important. Increased intragastric pressure tends to assist the valve mechanism having normal relationships by closing the valve, but, with the esophagogastric junction in the mediastinum, reflux readily occurs. Barrett [10] feels that the integrity of the muscularis mucosae, which moves the mucous membrane, must be intact. The muscosae slides on the muscularis externae and forms a flap which covers the esophageal orifice and thus closes the valve. The earliest changes that occur in esophagitis are not visible in the distal esophageal mucosae to the endoscopist's eye but are quite evident to the pathologist in the region of the muscularis mucosae in a biopsy specimen. Inflammatory changes and fibrosis will destroy the mucosa flap valve mechanism by destroying the muscularis mucosae. How many

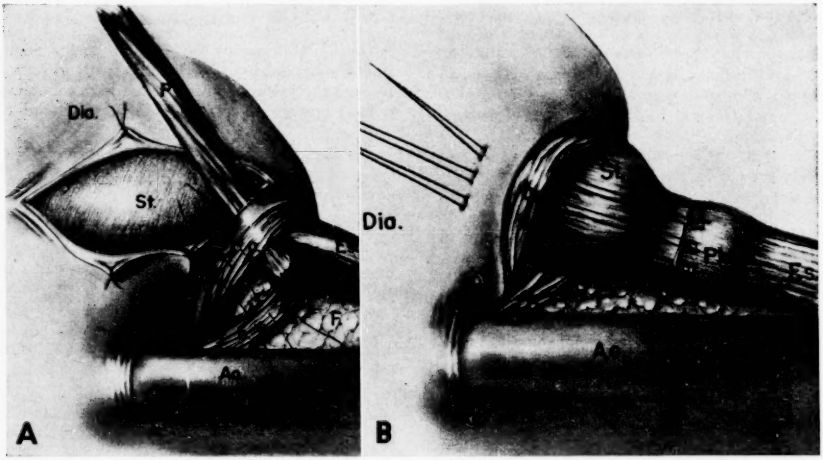

Fig. 2.—Illustration of operative area from left transthoracic approach. *A*, Penrose drain in place, with interrupted sutures placed posteriorly to approximate hiatal musculature and to narrow opening (*Ao*, aorta; *Dia*, diaphragm; *Es*, esophagus; *F*, mediastinal fat; *P*, Penrose drain, *St*, stomach; *b*, right crus of hiatus; *a*, left crus of hiatus). *B*, stomach herniated upward and phrenoesophageal ligament dissected free as membrane, with its insertion into esophagus preserved. Three sutures only (more are usually necessary) have been placed in ligament; both ends of each have been passed through hiatus and then through diaphragm from abdominal to thoracic side (*Ph*, phrenoesophageal ligament).

months or years are necessary to make these changes advance to a stage of irreversibility varies with the severity of the regurgitation and with the concentration of the irritating gastric juice.

Many "asymptomatic" persons have hiatus hernia demonstrated on barium x-ray examination with use of barium sulfate, but it is curious why they seek medical aid and have x-ray studies done. What initiates symptoms in persons with previously asymptomatic hiatus hernia is not known. We have noticed a strong correlation between the onset of symptoms with physical or emotional stress, prolonged hospitalization and recumbency, an operation not related to the stomach or esophagus, transient hyperacidity, repeated severe vomiting, and the prolonged use of an indwelling nasogastric tube.

Because of the terrifying consequences of an untreated and symptomatic hiatus hernia,[11] we strongly urge surgical repair before the irreversible changes in the submucosal layers occur. A period of adequate medical management should be tried first; however, unless the symptomatic trend is completely reversed and unless one is sure the patient will adhere to a strict medical program, surgery should be advised without procrastination.

In experienced hands either the abdominal or transthoracic approach can be used to accomplish an equally satisfactory operation. In many instances concomitant procedures can be done in the upper part of the abdomen, making this route preferable.[4] However, many surgeons today still fail to accept hiatus hernia as a cause of symptoms. During an abdominal operation a halfhearted attempt may be made at repairing the hernia, with strict attention to details not being followed, and the patient is not helped. This type of repair is mentioned only to be condemned and has nothing to offer other than antacids, bland diet, and antispasmodic drugs.

Our preference is for the transthoracic approach (fig. 2). The basic principles of an adequate repair should not be compromised; however, each surgeon has personal preferences in technical management, and these details should be varied according to necessity.

The basic principles are as follows: 1. The esophagogastric junction should be brought below the diaphragm and maintained there. 2. The peritoneal sac should be destroyed. 3. The phrenoesophageal ligament, if suitable, should be sutured to the abdominal surface of the diaphragm. 4. The fatty bare area posteriorly should be eliminated and the hiatus narrowed by approximation of the two muscular bundles of the right crus posteriorly. 5. The oblique angle of entrance of the esophagus into the stomach should be protected and maintained. If these principles are followed, the results, we feel, should be excellent.

Summary

The surgical treatment of hiatus hernia was evaluated in 65 patients. Medical management should be tried first, but, unless symptoms are relieved completely and the patient is willing to adhere strictly to a rigid medical management for many years, operation should be performed. Surgical repair resulted in 90.8% of the patients in this study becoming asymptomatic over a follow-up period of six months to seven years.

Close attention to details of the operation is mandatory for good results. The abdominal or thoracic approach can be used to accomplish the same technical results, but the basic principles should not be compromised. Our preference is for the transthoracic approach. The cardia must be reduced below the diaphragm. The hernia sac must be destroyed. The bare area posteriorly should be eliminated and the hiatus narrowed by approximation of the muscular bundles of the right crus posteriorly. The phrenoesophageal ligament should be sutured to the abdominal surface of the diaphragm, and the oblique angle of entrance of the esophagus into the stomach should be maintained.

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PRURITUS ANI ET VULVAE

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For purposes of this round table discussion on anogenital pruritus, we have reviewed our last 500 cases and the voluminous literature on the subject for the past 25 years. Concepts of this symptom complex have been constantly changing. The literature is replete with articles approaching the subject from the standpoint of the surgeon,[1] the gynecologist,[2] the dermatologist,[3] the allergist,[4] and the psychiatrist.[5] It is obvious that for the proper treatment a diagnosis must be made based on etiology. Local treatment, based on the symptom of itching, may be temporarily successful, but in the long run may lead to serious disappointments and complications.

Pruritus ani et vulvae is a symptom complex of great variation. Pruritus without any visible pathology exists only for a short period of time. Very soon, changes appear in the skin and the adjacent mucous membranes. The examiner must be able to recognize the basic inflammatory process in order to make an etiological diagnosis. He must be able to distinguish between a dermatitis due solely to scratch and a dermatitis due to primary chemical irritation and a dermatitis of allergic origin. He must also be able to recognize the earliest signs of atrophy, hypertrophy, and specific inflammatory processes such as occur in lichen planus, lupus erythematosus, and parasitic infestations.

Each specialist tends to overemphasize disturbances or diseases with which he is familiar as the cause of pruritus of the anogenital region. Vulvectomies for lichen planus and perianal injections of alcohol or tattooing for perianal psoriasis have been done after inadequate examination. Likewise, prolonged dermatological therapy for anogenital pruritus without benefit is carried out when the dermatologist fails to have adequate gynecologic and proctological examination for such things as cryptitis, proctitis, and cervicitis. In our experience, some of the worst treatment failures have occurred after months of therapy by a stubborn specialist who would not recognize the importance of other fields. We refer particularly to cases of pruritus vulvae due to an almost insignificant discharge from a focus of infection in the genital tract requiring the attention of a gynecologist and intractable pruritus ani treated for months by a dermatologist and found by the proctologist to be due to cryptitis in hidden pockets of infection. The following list is our classification of pruritus ani et vulvae based on etiology: (1) local primary irritation, (2) contact dermatitis (dermatitis venenata), (3) specific dermatological diseases, (4) anal, rectal, and genitourinary tract disease, (5) disease of other organs, and (6) psychogenic disturbances.

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Chairman's address, read before the Section on Dermatology at the 107th Annual Meeting of the American Medical Association, San Francisco, June 24, 1958.

Local primary irritation is by far the most frequent cause of pruritus ani et vulvae. Other causes are contact dermatitis, specific dermatological diseases, disease of the anal, rectal, and genitourinary tracts, disease of other organs, and psychogenic disturbances. Etiological diagnosis is often difficult because pruritus from any cause can exist for only a short time before visible secondary changes are induced by scratching and medication. Anal pruritus scarcely exists in geographical areas where bathing with water and no soap or toilet paper is the custom after defecation. When an organ system other than the anogenital apparatus is involved, all local sources of irritation should be removed and conservative treatment applied until the true source of the itching sensation becomes apparent. Presumed psychogenic disturbances are made worse by treatment if the diagnosis happens to be incorrect, and the supposed emotional exhaustion rapidly disappears when the real etiology is discovered and eliminated. More time should be spent on searching out the underlying cause of anogenital pruritus. Specific sensitization to condiments should not be overlooked in unsolved cases.

Local Irritation

The various sources of local irritation comprise by far the largest group. At first there is itching of various degrees followed by the development of a scratch dermatitis, with erythema, scaling, thickening, fissuring, hyperpigmentation, and, as a final stage, leukoplakia and possibly malignancy. The three commonest sources of irritation are (1) leukorrhea, even though minimal; (2) the daily use of toilet soap; and (3) the retention of fecal remnants in folds of the anal canal. A fractional drop of leukorrheal discharge from any cause, such as trichomonas vaginalis infection, can set up an intolerable itching which may be protracted over months and even years. In uncleanly people, who bathe infrequently, the retention of sweat and sebaceous material protects the skin and mucous

membranes from the irritating effects of this discharge. Protective ointments and pastes have proved effective in relieving the pruritus because of their protective effect.

It is an ironic and extremely important fact that anal pruritus scarcely exists in geographical areas where bathing with water and no soap or toilet tissue is the custom after defecation. Marchionini,[6] in 1952, stated that, because of the religious precepts of Islam, after defecation only plain water was used for cleanliness and all mechanical irritation of the skin and mucous membranes was avoided, thus eliminating a medium favorable to the growth of microbes. Fecal remnants were removed and, although hemorrhoids were common, irritation did not develop. In his own practice now, in Munich, he uses dilute potassium permanganate solution for cleansing purposes after defecation. This is a practice which we have used for more than 30 years for the entire anogenital area with gratifying results.

Highly alkaline soap precipitates retained in folds and crypts produce a chemical irritation which may last for one to two weeks and, because of daily repetition, may become progressively worse. Often retention of a combination of minute fecal material and soap precipitates the pruritus. It is our firm belief that primary irritation from the above-mentioned sources of irritation is the basis of at least 75% of all anogenital pruritus, although there may be secondary factors of great importance such as emotional stress.

Contact Dermatitis (Dermatitis Venenata)

Next to primary irritation, contact dermatitis is the most common cause of itching of the anogenital region. A large list of substances has been incriminated. The principal allergenic substances include local medications, toilet paper, suppositories, enema and douche nozzles, resin finishes on fabrics, drugs taken by mouth, nail lacquer, deodorants, plant oleoresins, contraceptives, and some foods. There are numerous reports in the literature of anogenital pruritus due to specific sensitization to common foods such as milk, wheat, eggs, chocolate, alcohol, fish, coffee, cocoa, beef, figs, tomatoes, asparagus, dewberries, beans, avocados, pork, prunes, peas, beets, yeast, chicken, rice, oranges, and peanuts. Some of these were confirmed with patch tests, some with intradermal tests, and others by the use of elimination diets. It has been our experience over many years that a positive patch or intradermal test is only another finding and that in all cases this must be proved clinically by withdrawal of the suspected food followed by a recrudescence after the food has been again ingested.

There is a vast difference between urticarial reaction to the protein fraction of foods and the development of a contact dermatitis due to specific epidermal hypersensitivity to an oleoresin. Urticaria due to the protein fraction of foods can always be elicited over other parts of the cutaneous surface and is never limited solely to the anogenital region. We believe that contact dermatitis due to oleoresins in certain foods and particularly condiments offers a fertile field for further investigation. We have yet to prove a localized anogenital pruritus due to specific sensitization to the oleoresins of common foods. However, we would at this time like to report a series of 11 cases of anogenital pruritus due to specific hypersensitivity to the oleoresins of condiments. Although spices have been mentioned as possible causes of pruritus ani et vulvae,[7] there are no published reports of confirmatory patch tests to any of the condiments. Mustard, pepper, cloves, cinnamon, anise, and nutmeg have been shown to be the cause of dermatitis of areas other than the anogenital region and, in some of these instances,[8] positive patch tests have been secured. In our series, in each case a battery of standardized patch tests was performed. This list included mustard, pepper, cloves, cinnamon, nutmeg, vanilla, and allspice. In each instance, where a positive patch test was secured, a flare-up of anogenital pruritus was produced on further ingestion of the suspected condiment.

The main clinical features of an anogenital pruritus due to specific sensitization to oleoresins are easily recognized. The itching begins perianally and shortly thereafter itching of the vulva and surrounding parts develops. There is a spreading contact type of dermatitis which first involves the intergluteal and perianal areas. Depending on the severity of the dermatitis, the entire area becomes confluent and the dermatitis may spread out to involve the thighs and the crural folds. In some cases, there is fluctuation in the severity, depending on the frequency of ingestion of the offending condiment. In our one black pepper case, the dermatitis was severe and continuous. In one of our cinnamon cases, the itching was pronounced for three or four days the first part of the week and subsided by the end of the week or until cinnamon was again ingested at Sunday morning's breakfast. There was wide variation in fluctuations in our mustard cases. Some were continuous, others with periods of freedom depending on the frequency of ingestion. It is well to remember that mustard is present in most salad dressings as well as meat sauces, ketchup, and chili sauce.

Contact dermatitis of the vulva without involvement of the anal area is not common. Substances commonly incriminated include local medications, suppositories, contraceptives, sanitary pads, tampons, douche nozzles, pessaries, nail lacquer, plant oleoresins, and certain medicaments excreted through the urine. All of these possibilities must be investigated when there is a dermatitis present. A unilateral contact dermatitis is sometimes due to specific hypersensitivity to nail lacquer and usually is on the left side due to contact with the fingernails of the right hand. A unilateral itching may be due to neurogenic causes, although careful investigation of all sources of irritation, including masturbation,

must be made. There may be a patchy dermatitis of the eyelids, cheeks, or neck, which are the common sites of nail lacquer dermatitis.

Other Dermatological Diseases

Space does not permit a full discussion of dermatological disorders which may involve the anogenital region and which require special dermatological training for diagnosis. These diseases include dermatitis medicamentosa (especially phenolphthalein), psoriasis, seborrheic dermatitis, neurodermatitis, mycotic infection, intertrigo (bacterial), miliaria, lichen sclerosis et atrophicus, kraurosis vulvae, parasitic infestation, lupus erythematosus, lichen planus, and leukemia cutis. It is obvious that the symptoms of anogenital itching requires a thorough dermatological examination and in many cases a biopsy and complete laboratory tests.

Anorectal Diseases

Anal itching has been attributed to many anorectal disorders. In our experience, the following signs are the most common causes of this symptom: cryptitis, hemorrhoiditis, fissures, sinuses, fistulas, proctitis, neoplasm, and polyps. If uncomplicated by injudicious treatment, the itching usually remains localized to the perianal area, but occasionally itching of the genital and scrotal areas develops. A scratch dermatitis appears which with the passage of time becomes a chronic dermatitis with thickening, fissuring, and hyperpigmentation. In addition to a careful proctological examination, one must never forget that primary irritation from retained fecal material and soap in many folds and crypts may be the sole cause of inflammation of the anal ring.

Disease of Organs Other Than the Anogenital Region

Many general diseases have been incriminated as the cause of itching of the anogenital area. The commonest one in our experience is urticaria. In some patients who have occasional bouts of urticaria, their skins are in a constant subthreshold stage of urticaria. These patients develop itching of the anogenital area with extreme ease, and careful examination will elicit the basic nature of the condition with evidences elsewhere of urticaria. Endocrine diseases, including thyroid, pituitary, ovarian, and pancreatic (diabetes) have been incriminated. Neurological disturbances such as autonomic imbalance and epilepsy have been accompanied by anogenital pruritus. Other diseases mentioned in the literature include hepatic disease, renal disease, prostatitis, cystitis, appendicitis, intestinal parasites, bladder stone, vesiculitis, disease of the uterus and adnexa, lymphoma, and allergic rhinitis. We believe that in all cases where an organ system other than the anogenital apparatus is involved all local sources of irritation should be removed and conservative treatment applied until the true source of the itching sensation becomes apparent.

Psychogenic Disturbances

Three American textbooks of dermatology [9] attribute the majority of cases of pruritus ani et vulvae to some psychogenic disturbance. Their terminology varies. Many highly qualified dermatologists stress the importance of emotional factors in anogenital itching. We agree that emotional factors sometimes play major roles in anogenital itching. We believe that all emotional stress accentuates, prolongs, and magnifies the symptom of itching. However, we are firmly convinced that a careful history and thorough examination will show that psychogenic factors are secondary in the vast majority of cases. What would be a mild, insignificant pruritus ani or pruritus vulvae in an emotionally stable individual could be magnified to a major disaster in another individual under intense emotional stress. Not enough attention has been paid to the primary trigger mechanism. More careful attention to the primary cause of the itching will eliminate a large percentage of the so-called psychogenic anogenital pruritus cases. The theory that pruritus ani et vulvae is a type of hysteria in which the gratification of pruritus is analogous to gratification of libido and the pain of scratching is related to self-punishment and guilt [10] does not succeed in curing a middle-aged woman of pruritus of the anogenital region when the cause of her pruritus is a low-grade leukorrhea and washing of the parts three or four times daily with soap.

Another popular approach regards pruritus ani as a hypochondriacal syndrome based on the failure to successfully repress infantile fantasies concerning procreation and anal birth.[5] This has the appearance of picking a needle out of a haystack. In one of our pepper cases, that of the wife of a physician, and in one of the mustard cases, that of a middle-aged spinster, as well as in many of the routine cases due to leukorrhea and irritation from soap, the patients had already had a diagnosis of psychogenic or emotional basis for the cause of their itching. It has been our observation that many of these patients subjected to long, drawn out treatment for presumed psychogenic disturbances are made infinitely worse. It is startling how rapidly the emotional exhaustion disappears when the real etiology is discovered and eliminated. We would urge that much more time be spent on searching out the underlying cause of anogenital pruritus and its elimination.

Summary

The treatment of anogenital pruritus depends on the determination of the cause of the pruritus. More attention must be given to a search for primary irritants, such as the use of soap, leukorrhea, retained fecal matter, and local medications. Contact dermatitis due to specific hypersensitivity is a distinctive entity and its cause must be determined. Oleoresins in condiments should not be overlooked. Specific dermatological diseases of the anogenital area must be correctly diagnosed and treatment

based thereon. The gynecologist and proctologist need consultation with the dermatologist and certainly the reverse holds true. Anogenital pruritus in some cases may be but a symptom of an internal medical condition. Psychogenic disturbances and emotional stress are always a factor in anogenital pruritus, but they should never be assigned the primary etiological role without complete examination and consideration of all other possible causes.

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ADVERSE REACTIONS TO SULFAMETHOXYPYRIDAZINE (KYNEX)

ITS USE IN THE TREATMENT OF DERMATITIS HERPETIFORMIS

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In most cases the control of dermatitis herpetiformis may be readily achieved with sulfamethoxypyridazine. It is impossible to predict the level of maintenance dose necessary to suppress the clinical reaction, and it is similarly impossible to predict the blood levels achieved with any single unit dosage. Adverse reactions deter from the over-all usefulness of the drug. The adverse reactions observed concerned principally the skin and hematopoietic system. In addition, the gastrointestinal and central nervous system showed evidence of toxicity. The dermatological manifestations followed almost all known previously reported reactions to sulfonamide drugs. The administration of this drug requires routine assay of the blood for sulfamethoxypyridazine levels. It is the duty of the clinician to balance the benefits to be derived from any drug against the risks of its administration.

The administration of any drug to a patient is fraught with the possibility that undesirable and adverse reactions may ensue. The clinical usefulness of any drug, once the therapeutic indication has been determined, depends to a very considerable extent on whether it is likely to produce more than a minimal number of reactions when a large number of patients take the drug. If a drug fulfills a sufficiently critical therapeutic role it may continue to be prescribed despite a rather large number of undesirable reactions. It is the duty of the clinician to balance the benefit to be derived from the drug against the risks of its administration.

The administration of sulfamethoxypyridazine (Kynex) to a group of patients with dermatitis herpetiformis whose disease was otherwise incompletely controlled by other modalities of treatment resulted in a gratifying response in a sufficiently large proportion of the patients treated to suggest its further use in this disease. The advantages of

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sulfamethoxypyridazine administration were the beneficial results achieved in a majority of the patients treated and the simplification of the therapeutic program, inasmuch as treatment for the most part was given only once a day.

Data

The treatment of 20 patients with dermatitis herpetiformis represents a part of our experience with sulfamethoxypyridazine. The only criterion used in the selection of patients for inclusion in this group was that they presented the clinical morphologic picture of dermatitis herpetiformis. In some instances this clinical impression was fortified by results of skin biopsy that were compatible with the diagnosis of dermatitis herpetiformis, by patch-test reactions to anion members of Hofmeister's series, and by eosinophilia of the peripheral blood. The data on these 20 patients are summarized in table 1.

TABLE 1.—*Summary of Data on Twenty Patients with Dermatitis Herpetiformis Treated with Sulfamethoxypyridazine*

Case, No.	Sex	Age, Yr.	Duration of Disease, Yr.	Control	
				Results	Dosage, Gm.
1	M	65	15	Incomplete	...
2	F	57	6	Incomplete	...
3	M	62	1½	Good	2.5/day
4	F	66	20	Good	0.5/day
5	M	46	14	Incomplete	
6	F	37	6	Good	1/day
7	F	63	25	Good	0.125/day
8	M	44	5	Good	1/day
9	M	19	1¾	Good	Adverse reaction
10	F	60	2	Incomplete	...
11	F	37	1	Good	0.5 in a. m.; 0.25 in p. m.
12	M	60	8	Trial unsatisfactory	...
13	M	25	8	Good	0.25 twice a day
14	M	44	1½	Good	Adverse reaction; died
15	M	45	20	Good	0.5/day
16	M	28	9	Good	0.5 every 2 or 3 days
17	M	56	¼	Good	1 every other day; 0.5 on alternate days
18	M	47	9	Good	Adverse reaction
19	F	3	7/12	Failure	...
20	M	59	3	Good	Adverse reaction

Thirteen of the 20 patients were males, the majority being in the fifth, sixth, and seventh decades of life; the ages ranged from 3 to 66 years. Only two patients had dermatitis herpetiformis for less than a year, with 13 of the 20 patients having had their disease for three years or longer. Thus, most of the patients had been subjected to a variety of treatments prior to the initiation of therapy with sulfamethoxypyridazine. The periods of follow-up varied from 2 to 11 months.

Early in the course of the study, because of a lack of appreciation of the fact that the drug would accumulate in the blood, therapy was administered in a manner similar to that employed with other sulfonamide drugs. Later it was our practice to administer 1 Gm. of sulfamethoxypyridazine during the first 24 hours of treatment, followed thereafter by 0.5 Gm. per day. Adjustment in the dosage schedule was made subsequently in accordance with the patient's clinical response.

Blood levels of sulfamethoxypyridazine were determined consistently on the patients seen during the latter part of the study, as it was recognized by tests on individual patients seen earlier that variable blood levels occurred with standard dosage schedules. For illustration, the patient in case 3 was dismissed from our care with his dermatitis herpetiformis controlled; he was instructed to continue taking 1 Gm. of sulfamethoxypyridazine a day. He subsequently recognized that this afforded an inadequate suppressive effect and on his own initiative increased his daily intake to 1.5 Gm. Still later, he took 2 Gm. routinely and, occasionally, even 2.5 Gm. per day for the desired relief. After approximately three months on this increased dosage, the concentration of sulfamethoxypyridazine was 8.7 mg. per 100 cc. of blood. On the other hand, in the patient in case 8, who took 1 Gm. of sulfamethoxypyridazine per day for three months, a concentration of 11.4 mg. per 100 cc. of blood developed.

The results of treatment of these 20 patients might be summarized as follows: good continued response, 10 patients; good response but subsequent reaction, 4; incomplete control, 4; failure, 1; and unsatisfactory trial, 1.

Control of the symptoms of pruritus and burning and eradication of the cutaneous eruption occurred in 10 of the 20 patients. By "incomplete" control we would indicate that sulfamethoxypyridazine alone was inadequate to control the eruption but when it was combined with other modalities of therapy the signs and symptoms of the disease were abated. The dosage varied from as little as 0.5 Gm. every two to three days to 2.5 Gm. per day. The usual dosage, however, was 0.5 Gm. per day taken as a single dose. The details of treatment in case 17 are presented to illustrate a good response to the treatment and to demonstrate the laboratory evaluation carried out.

CASE 17.—A blistering eruption had developed in a 56-year-old man three months previous to admission. The eruption took the configuration of grouped bullae over the extensor surfaces of the arms, the anterior and posterior parts of the thorax, the buttocks, and the inguinal areas, and about the extensor surfaces of the knees. Rather intense pruritus and burning of the skin were associated symptoms. Prior to his being seen by us, steroid therapy had been administered without benefit.

The diagnosis of dermatitis herpetiformis was established on the basis of the clinical morphology of the eruption and a skin biopsy which showed a pressure or tension bulla without evidence of acantholysis.

Therapy was initiated with sulfamethoxypyridazine in a dosage of 0.5 Gm. given twice the first day and 0.5 Gm. given daily thereafter. Table 2 indicates the dosage of the drug and the blood levels achieved. On this dosage schedule there was good control of the dermatitis herpetiformis (fig. 1). During the period of observation blisters recurred a few times but these periods have been short-lived. On each of these occasions the patient could relate the relapses to long periods of hard physical labor.

Sulfamethoxypyridazine was given a clinical trial in nine patients with other dermatological diseases as follows: bullous pemphigoid, four patients; erythema multiforme, three; eczema nummulare, one, and lichen planus, one. A hemolytic process secondary to sulfamethoxypyridazine therapy developed in one of these patients, and her case will be presented in detail later in this paper. The lack of response to therapy in this group led us to believe that sulfamethoxypyridazine possesses no specific propensities for ameliorating dermatological diseases but that its therapeutic effectiveness is the antibiotic property ascribed to the sulfonamide group as a whole.

TABLE 2.—*Dosage and Blood Concentration of Sulfamethoxypyridazine in Patient in Case 17*

Date	Dosage, Oral, Gm.	Sulfamethoxypyridazine Level, Mg./100 Cc.
1/22	0.5 twice a day for 1 day; 0.5 a day thereafter	...
1/28	0.5 a day	2.4
2/5	1 twice a week; 0.5 on other days	4.5
3/25	1 every other day; 0.5 on alternate days	3.9
4/22	1 every other day; 0.5 on alternate days	5.3

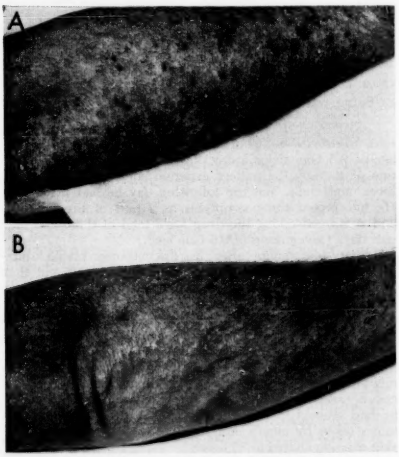

Fig. 1 (case 17).—Dermatitis herpetiformis: *A*, before treatment and, *B*, after 12 days of treatment with sulfamethoxypyridazine. This patient subsequently had leukopenia secondary to drug therapy.

Adverse Reactions

Adverse reactions to sulfamethoxypyridazine were encountered in some of the patients. Such reactions will, of course, detract from the over-all usefulness of the drug. Close observation of the patient during administration should, however, give early recognition to potentially serious reactions and prevent fatalities from occurring.

During the Second Conference on Sulfonamides, Lehr [1] reviewed the clinical toxicity of sulfonamides and listed the reactions as follows: (1) potentially serious reactions, including complications of the urinary tract, sensitization reactions (drug fever, rash, and contact reactions), blood dyscrasias, and hepatitis, and (2) milder reactions, including acidosis, cyanosis, and reactions related to the central and peripheral nervous systems.

It is interesting to note that, among the potentially serious reactions listed, only complications of the urinary tract have been unreported to date. Drug fever and cutaneous eruptions have been commonly reported, with headache and other complaints related to the central nervous system being not uncommon.

TABLE 3.—*Incidence of Adverse Reactions to Sulfamethoxypyridazine as Reported in Literature*

Author	No. of Cases	Reactions No.	%	Types
Jones, W. F., and Finland, M.: Ann. New York Acad. Sc. **69**:478, 1957	6	0	...	...
Lepper, M. H., and others: Ann. New York Acad. Sc. **69**:485, 1957	49	0	...	...
Jackson, G. G., and Grieble, H. G.: Ann. New York Acad. Sc. **69**:493, 1957	56	5	8.9	Headache, fever, eruption, abdominal pain, dizziness
Ross, S., and others: Ann. New York Acad. Sc. **69**:501, 1957	14	0	...	...
Walker, W. F., and Hamburger, M.: Ann. New York Acad. Sc. **69**:509, 1957	52	1	1.9	Eruption
Songco, R. S., and others: J. Philippine M. A. **33**:520, 1957	36	3	8.3	Vomiting, cutaneous eruption
Velasco-Joven, E. K., and Domingo, P.: J. Philippine M. A. **33**:584, 1957	3	0	...	...
Grieble, H. G., and Jackson, G. G.: New England J. Med. **258**:1, 1958	63	4	6.4	Headache and maculopapular eruption common; also fever, abdominal pain, dizziness
Lindsay, D. G., and others: A.M.A. Arch. Dermat. **78**: 299, 1958	85	13	15.3	Severe bullous eruption; other eruptions

Table 3 summarizes the clinical experience of other investigators with sulfamethoxypyridazine and the incidence of complications with this therapy. Tisdale [2] recently reported the additional complication of focal hepatitis in a patient receiving sulfamethoxypyridazine.

We observed a total of 28 patients—19 with dermatitis herpetiformis (one of the 20 patients had an unsatisfactory trial) and 9 with assorted dermatological conditions—and in this series five adverse reactions occurred. Case 14 was included in a preliminary report.[3] Sulfamethoxypyridazine afforded good control of this patient's dermatitis herpetiformis; however, pyrexia, arthralgia, and albuminuria developed, and these were interpreted as manifestations of a toxic reaction rather than a true reaction of hypersensitivity. When this patient

was dismissed from the clinic, his general health was considered good and laboratory evaluation reflected no abnormal finding. He died about 10 days later but, because autopsy was not performed, we can only speculate on the course of events.

The patient in case 9 had an initial good response to treatment with sulfamethoxypyridazine, but on his return home a generalized erythematous maculopapular eruption developed. The patients in cases 18 and 20 each demonstrated an initial good control of the disease, only to manifest subsequently an adverse reaction characterized by leukopenia. The details of case 18 follow.

CASE 18.—A 47-year-old man gave a history of a pruritic eruption, consisting of grouped vesicles and urticarial papules over the scalp, thorax, scapular areas, abdomen, and extensor surfaces of the elbows and knees, that had been present for about nine years. A diagnosis of dermatitis herpetiformis was made on the basis of the morphology of the skin lesions and a skin biopsy which showed pressure or tension bullae without evidence of acantholysis. In addition, patch tests with potassium iodide gave a positive reaction, and the eosinophil count on the peripheral blood was 3.5%. A variety of medicaments given systemically in the past had not achieved control of the condition. More recently, steroids had been tried without success.

TABLE 4.—*Dosage, Blood Concentration of Drug, and Leukocyte Count in Patient in Case 18*

Date	Dosage, Oral, Gm. per Day	Sulfamethoxypyridazine, Mg. per 100 Cc.	Leukocytes per Cu. Mm.
1/16	0.5 twice; 0.5 thereafter	...	5,400
1/22	0.75	3.9	4,000
1/28	0.75	2.1	4,000
2/13	0.75	2.1	3,100
2/20	0.75	2.3	3,700
3/13	1	2.6	4,100
4/12	Discontinued	3.3	2,800
4/24	...	0.15	4,200

When the patient was first seen, sulfamethoxypyridazine was administered in a dosage of one tablet (0.5 Gm.) twice a day for one day and then one tablet per day thereafter. Lack of complete control later necessitated increasing the dosage of the drug. Table 4 indicates the oral intake of the drug, the concentration of the drug in the blood, and the leukocyte counts.

While the patient was receiving sulfamethoxypyridazine, his dermatitis herpetiformis remained under good control. However, after a month of treatment with a dosage of 1 Gm. per day and the attainment of a leukocyte count of 2,800 per cubic millimeter of blood, it was considered that he had a toxic suppression of the leukocytes and treatment was discontinued. A subsequent course of sulfamethoxypyridazine therapy has not been attempted.

In the group of patients with miscellaneous diseases who were treated with sulfamethoxypyridazine, there was one in whom a hemolytic process developed, most probably on the basis of use of this drug. A summary of this case follows:

CASE 21.—A 64-year-old woman was admitted directly to the hospital for treatment of a generalized cutaneous blistering eruption that had been present for four months. Mucosal lesions had never been evident.

On admission, she presented a widespread bullous eruption without particular grouping; some of the bullae were seen to be arising from normal skin, while others were on an urticarial base. She had marked pruritus. Pertinent laboratory evaluation included a skin biopsy which showed a tension or pressure bulla without acantholysis. A definite diagnosis was not established. Thus, a variety of treatments, including use of sulfapyridine, diphenhydramine (Benadryl) hydrochloride, sulfamethoxypyridazine, and steroids, was instituted.

Because of lack of response to any one of these medications, a second course of sulfamethoxypyridazine therapy was given about three weeks after she had received the first course; this course consisted of 2 Gm. of the drug given daily in a single dose for eight days. Only partial control of the blistering was achieved.

On this dosage schedule the blood level of sulfamethoxypyridazine was 19 mg. per 100 cc. on Dec. 5, 1957, and, thus, administration of the drug was discontinued. When the level reached 3.5 mg. six days later, the drug was again administered in a dosage of 0.5 Gm. per day, and this dosage was continued for six additional days.

When the patient was admitted on Oct. 28, the hemoglobin level was 12.6 Gm. per 100 cc. of blood; on Dec. 3 and Dec. 7 it was 9.7 Gm.; and on Dec. 16, the day treatment with sulfamethoxypyridazine was permanently discontinued, it was 8 Gm. There was no corresponding decrease in the leukocyte count. The reticulocyte count on Dec. 16 was 7.2%. After two transfusions of 500 cc. of whole blood and inauguration of the daily administration of iron by mouth, there was a return of the blood value to normal within the next month.

The physicians of our clinic group referred patients with adverse cutaneous reactions from sulfamethoxypyridazine to us for dermatological consultation. A summary of one such case is given here because the case illustrates perhaps the commonest cutaneous reaction as recorded by those reporting adverse reactions to this drug.

CASE 22.—A 26-year-old man was treated for an "influenza syndrome" with sulfamethoxypyridazine given in a dosage of 0.5 Gm. twice a day. Twenty-four hours after initiation of therapy the patient experienced increased lassitude, fever, and chills, and the following day he had headaches. He interpreted these symptoms as a part of the influenza and continued taking the drug for a total of three and one-half days (seven doses of 0.5 Gm. each).

Twenty-four hours after he discontinued taking sulfamethoxypyridazine only general malaise persisted, but then a generalized, fine, erythematous maculopapular eruption developed which was accentuated on the trunk (fig. 2). No oral lesions were present. At this time (two and one-half days after use of the drug had been stopped) the blood level of sulfamethoxypyridazine was 5.4 mg. per 100 cc.

The patient gave no history of hay fever, asthma, or migraine headaches. A sulfonamide drug had been taken on one occasion previously without reaction, but in the past he had reacted to penicillin with urticaria. With antihistamines taken by mouth and soothing topical treatments, the skin reaction abated in 72 hours.

The entire group of sulfonamide drugs is known to produce fixed drug reactions, and sulfamethoxypyridazine is no exception in this regard. To our knowledge, a fixed drug reaction has not previously been reported, although there is no reason to presume it would not eventually occur.

CASE 23.—A 29-year-old woman had been receiving care for recurrent infections of the urinary tract. Prophylactic treatment with sulfamethoxypyridazine had been advised in a dosage of 0.5 Gm. given daily on five successive days during every two-to-three-week period. Her dermatological complaint was of an intermittent presence of a pruritic ery-

thematous plaque on the dorsum of the right third finger; this condition would persist for five to seven days and then disappear (fig. 3). It was only after direct questioning that she associated the skin eruption with the ingestion of sulfamethoxypyridazine. We interpreted her skin eruption as due

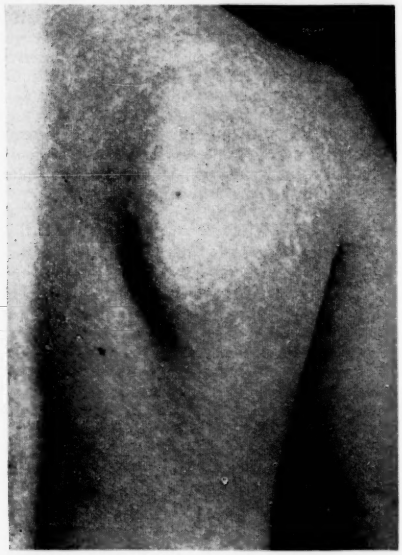

Fig. 2 (case 22).—Erythematous maculopapular eruption seen secondary to treatment with sulfamethoxypyridazine for influenza.

to a fixed drug reaction. She had taken sulfonamide drugs previously without untoward reaction. She gave no history of hay fever, asthma, migraine headaches, or urticaria.

Reactions of photosentivity can be anticipated in patients taking the sulfonamide drugs. A summary of such a case follows:

Case 24.—A 61-year-old farmer had had intermittent sore throat for four months. Among the drugs prescribed were tetracyclines, to one of which a cutaneous reaction developed. About five weeks prior to consultation with us, the patient took sulfamethoxypyridazine in a dosage of two tablets (1 Gm.) the first 24 hours and one tablet a day for the next four days. After this course of treatment an eruption developed on the sun-exposed portion of the body; this occurred during the period he was spending much time in the sun preparing his farm land for spring planting. Examination disclosed an eczematoid reaction of the face and ears (with sparing of the forehead) and of the dorsum of the hands and forearms. This patient gave no history of atopy but had previously had adverse reactions to a tetracycline preparation and to succinylsulfathiazole (Sulfasuxidine).

The employment of sulfamethoxypyridazine by us and other physicians, and our seeing the subsequent development of adverse reactions in some of these patients, alerted us to the fact that the drug was not without the potentialities of producing still other reactions which might in themselves be a more serious threat to the life of the patient than the original disease under treatment.

Comment

The unique pharmacological properties of sulfamethoxypyridazine are its low degree of acetylation and its slow renal clearance. The acetylated form is cleared faster from the blood than is the nonacetylated form. This medicament shares with sulfapyridine, sulfoxone (Diasone) sodium, and Promacetin (sodium 4, 4′-diaminodiphenylsulfone-2-*N*-acetylsulfonamide) a low degree of acetylation. The fact that drugs which suppress dermatitis herpetiformis have a common pharmacological property is of interest. The pharmacology and physiology of sulfamethoxypyridazine have recently been reviewed.[4]

In most cases the control of dermatitis herpetiformis may be readily achieved with sulfamethoxypyridazine. This control can be maintained with

Fig. 3 (case 23).—Fixed eruption occurring over dorsum of right third finger in patient taking sulfamethoxypyridazine as prophylaxis against recurrent infections of urinary tract.

low daily doses in most instances. Occasionally, a patient has taken as much as 2.5 Gm. a day to control his eruption without suffering ill-effects. The control is as good as that exercised by any of the other suppressive drugs used in the treatment of dermatitis herpetiformis.

The maintenance of high blood levels for 24 hours on a single dose of the drug as a result of its low renal clearance is of tremendous help in suppressing the eruption. In these circumstances it is possible for the patient to take one dose of the drug daily and for control to be maintained. It is a great convenience to patients, and, consequently, it is easier to gain their cooperation.

Just as it is impossible to predict the level of maintenance dose necessary to suppress the clinical reaction, it is similarly impossible to predict the blood levels achieved with any single unit dosage. While blood levels of 2 to 4 mg. per 100 cc. were obtained in most patients on daily maintenance doses of 0.5 Gm. of the drug, in some instances high blood levels were obtained with exactly similar dosages and in one instance a patient who was taking 2.5 Gm. per day had a relatively low blood level. Because of the danger of cumulative concentrations with the drug, routine studies of the blood and routine urinalyses should be made and also blood levels of sulfamethoxypyridazine need to be determined at various intervals to correlate the surface control with the unit dosage and the blood level achieved with that dosage. It seems apparent that this is the only safe way to administer this medicament over a long period.

The adverse reactions observed concerned principally the skin and hematopoietic system. In addition, the gastrointestinal and central nervous systems showed evidence of toxicity, as was described. The dermatological manifestations followed almost all known previously reported reactions to sulfonamide drugs. They all responded promptly to cessation of treatment with the drug and institution of appropriate therapeutic measures. No crystalluria has been observed. One original difficulty in the use of this medicament was the development of toxic reactions due to high blood levels. This included malaise, arthralgia, fever, and eruption. This type of reaction was perhaps the most serious encountered. There is no way of knowing precisely whether it contributed to the death of the one patient who, three weeks after having such a reaction and recovering satisfactorily as far as clinical and laboratory evidence was concerned, died suddenly under unusual circumstances described by the home physician as indicative of adrenal exhaustion.

The adverse reactions limit the usefulness of sulfamethoxypyridazine in therapeutic dermatology. However, it should be noted from the other series reported in table 3 and from our experience that the drug may be administered with a certain degree of safety once the method of administration is understood and treatment is given with appropriate safeguards, namely, determinations of the blood level of the drug, studies of its hematopoietic effects, and analyses of the urine. Without such safeguards it is obviously impossible to gauge the effectiveness of the medication or the possibilities of potential reaction. Drug reactions have always been a part of the administration of sulfonamide medicaments. In many instances they have been an accepted risk because of the usefulness of the particular medication. Sulfapyridine has an extremely poor pharmacological reputation. Yet, it is used routinely in dermatology for the suppression of dermatitis herpetiformis. We recently observed one patient who took 20 grains (1.29 Gm.) of sulfapyridine three times a week for 14 years without incident. The amount of sulfapyridine that is used in dermatology, in spite of the apparent pharmacological hazards, indicates that a drug may be useful in certain areas of medicine once its limitations and dangers are fully appreciated.

Summary and Conclusions

Adverse reactions to sulfamethoxypyridazine in this study were due to the toxic effect of cumulative dosage; these involved principally the hematopoietic and cutaneous organs. To our knowledge, a fixed drug reaction and the reaction of photosensitivity to sulfamethoxypyridazine have not previously been reported.

Sulfamethoxypyridazine was found to afford good control of dermatitis herpetiformis in 10 of 20 patients. Therapeutic control of the eruption was achieved in most instances with a single daily maintenance dose. There is no predictability in the relationship between the dose administered and the blood level obtained over long periods. Therefore, the administration of this drug requires routine assay of the blood for sulfamethoxypyridazine levels.

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CLINICAL NOTES

PRESERVATION OF NATURAL LANDMARKS IN UNILATERAL CLEFT LIP

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The harelip deformity, with its twisted distortion of the nose and gaping cleft of the lip, utterly disfigures the center of the face and destroys any chance of normal expression—even a smile is grotesque. So horrible is it that whatever the surgeon does will be an improvement. Yet, mere improvement is not enough and should not be accepted as a triumph. Rather, it is felt that, until these anomalies can be prevented, the surgical approach must be designed artistically so as not only to obtain a closure of the cleft but to camouflage it.[1]

Five years ago there was a constant trickle of patients with harelip to Kum Chon Korean Hospital, which services the population from a multitude of hutted villages in an area north of Seoul. Various degrees of this deformity were represented, and, after months of exposure to and stimulation from the problem, it began to dawn on me that all components of a normal lip and nose were more or less present in each person with cleft lip, depending on the severity of the deformity.

The Operation

If this were true, the primary step in construction would be to recognize all existing landmarks and juggle them out of distortion into normal position. Closer observation revealed, on the noncleft side, two-thirds of the cupid's bow, one philtrum column, and the associated dimple. As an entity they are drawn up toward the columella in an almost unrecognizable distortion (fig. 1*X*), but they are available and should be brought into use by a rotation incision under the columella that will drop the entire component *A* into correct position (fig. 2). This action will leave a triangular gap under the base of the columella which can be filled by a triangular advancement from the cleft side.

The cleft side, being primarily deficient, should not be called on to do more than is absolutely necessary. Yet, quite effectively and without undue strain, it can produce from its upper portion an adequate triangular flap to match the rotation gap. Of course, when the cleft is incomplete the bridging portion easily forms the leading point of the triangular flap *B* (fig. 2*W*). When the cleft is wide, a relaxing incision under the alar base is carried up into the nostril floor to pick up the point of the triangular flap *B*, which is to be advanced from the lateral lip element (fig. 2*X*). The advancement of this lateral triangular flap *B* not only fills the gap under the columella but also has a narrowing effect on the flaring alar base and wide nostril floor (fig. 1*Y* and *Z*). To facilitate this lateral advancement

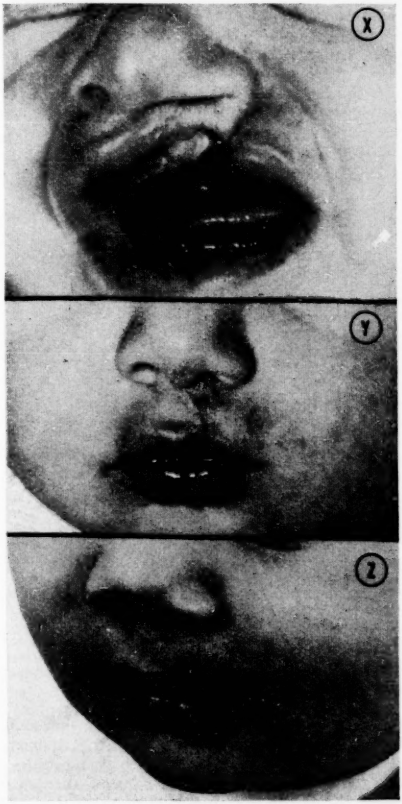

Fig. 1.—*X*, natural landmarks are distorted but present. *Y*, one month after surgery, cupid's bow and philtrum dimple have been maneuvered into normal position. Curving scar is still angry and slightly contracted. *Z*, three months later the scar has paled, smoothed out, and all but disappeared into the philtrum line.

From the Department of Surgery, University of Miami School of Medicine.

the lip and nose on the cleft side must be freed from their attachment to the maxilla by extensive undermining. Closure must be meticulous and pinpoint accuracy achieved in the approximation of the cleft at the white rolled edge of the cutaneous junction with vermilion. Chronic catgut sutures, 00000, are used in the muscle and mucosa membrane and silk sutures, 000000 in the skin.

Postoperative Care

A Logan bow is applied to protect the lip during the healing phase, and the suture line is sealed off from nasal discharge with bacitracin ointment three times daily.[2] Formula feedings are resumed as described by MacCollum and Richardson [3] with a 1½-in. extension of soft rubber catheter fitted to the end of a 10-cc. Asepto syringe. The catheter is eased in over the tongue, and constant pressure on the bulb produces a gentle flow of formula without the necessity of the healing lip puckering into traumatic sucking movements. The arms are restrained to keep the hands out of the mouth, and in the more acrobatic babies the legs are restrained to keep the feet out. On the fourth postoperative day the skin sutures are removed, and after one month the mother is instructed in gentle massage of the lip scar against the underlying gum with lanolin. For many weeks the scar will be hard, red, and slightly contracted (fig. 1*Y*), but as the months pass it will soften, relax, and pale out until it is almost invisible in its position as a philtrum line (fig. 1*Z*).

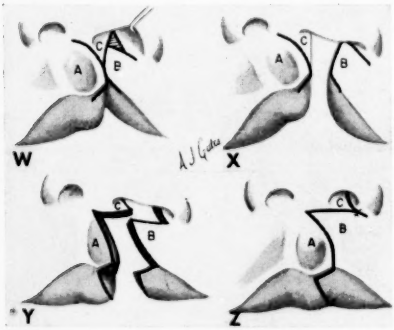

Fig. 2.—*W*, in incomplete clefts, lateral advancement flap *B* incorporates Simonart's band as its leading point. *X*, in complete clefts the lateral advancement flap *B* is developed by relaxing incision under alar base and picks up its leading point from lateral nostril floor. *Y*, flap *A* is rotated down and flap *B* advanced across cleft into rotation gap. Little flap *C* completes puzzle by interdigitating across floor of nose to straighten deviated columella, form nostril sill, and shoulder part of tension of lateral advancement. *Z*, Cupid's bow and entire philtrum dimple are now in normal position. Alar flare has been corrected. Resulting scar first curves to imitate the opposite philtrum column, then zig-zags out of sight as nostril sill and into nasal floor.

Timing the Operation

The optimum time for closure of cleft lip varies. If the deformity is minimal, operation can follow birth by a few hours. In my opinion this dash from womb to operating room is unnecessary, no matter how urgent the cosmetic emergency may seem. With an Asepto harelip feeder, feeding is no problem. Anxious parents can be pacified if it is explained that not only will the infant withstand anesthesia and operation better at 1 month of age but a more perfect lip and nose correction is likely to result.

If the cleft is severely wide, I feel it is extremely important to let the infant's tissues grow and enlarge for at least three months, after which surgical closure is relatively simple. When there is an associated cleft of the palate the principle of early closure as championed by Kilner [4] is favored. Palate clefts, in my opinion, should be corrected before the child begins to talk, anywhere from 10 to 12 months, depending again on the severity of the cleft. A gentle, well-planned operation should have minimal effect on the growth of the facial bones and still provide the child, from the outset, with an adequate mechanism with which to develop normal speech.

Summary and Conclusions

It never ceases to be a thrill that two simple incisions can set up a consecutive chain of happy actions: 1. The cupid's bow component, carrying with it one philtrum column and the entire dimple, drops into normal position, leaving a triangular gap above. 2. Advancement of the lateral lip element to fill this gap not only narrows the alar flare and wide nostril floor but unites the cleft along a curving line which simulates the one missing link, the matching philtrum column.

Several popular methods in use today ignore one or more of nature's landmarks and, what seems even more tragic, by actually destroying them in the primary repair cause them to be lost forever.

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AN IMPROVED VAGINAL APPLICATOR

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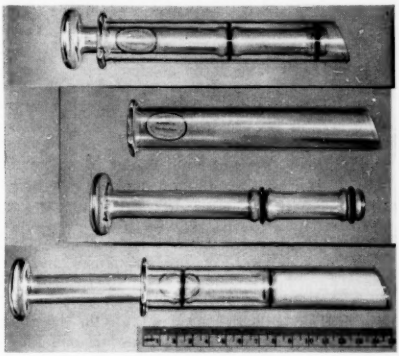
The office treatment of vaginal disorders by the local application of various powders, creams, and jellies is common practice. Most of the jellies, creams, and such are injected with syringe-type applicators usually supplied by the pharmaceutical manufacturers of the drug being used.

The placement of different powder preparations is not satisfactory, as a rule. The plastic squeeze containers, which are used to blow a stream of powder into the vagina, succeed in filling the speculum, but a minimum amount of the powder remains in the vagina itself. Another type, which blows up the vagina under pressure and forces the powder in simultaneously, seems too dangerous for use. The applicator shown (see figure) was designed to overcome certain difficulties. It will deliver a definite measured amount of any kind of preparation to the far end of the vagina without the slightest waste, under no pressure, and with no discomfort to the patient. It should be remembered, however, that some risk accompanies the use of this or any other such device in pregnant women. No instance of trouble, such as embolism, has thus far occurred in such cases with this device, but the possibility should be kept in mind.

It is a syringe made of heavy Pyrex glass, with a beveled end to facilitate insertion (see figure, *top*). The plunger, when pushed in as far as possible, automatically stops and simultaneously empties the barrel completely (see figure, *center*). The plunger has two neoprene rubber rings so arranged that the glass of the plunger does not touch the inside of the barrel. The applicator is easily sterilized and would be hard to break.

To use, the plunger is withdrawn and a little lubricant jelly is placed on each neoprene ring and the plunger replaced. The chosen amount of the selected medicament is then put in the barrel with the plunger drawn back (see figure, *bottom*), the tip of the barrel is lubricated slightly, and the tip is then inserted to the proper location, the plunger pushed all the way down, and the syringe withdrawn.



Top, applicator almost closed. When plunger is pushed in as far as possible, barrel is automatically emptied. *Center*, note construction of plunger. Glass side of plunger does not come in contact with inside of barrel and rides squarely on the two rings. *Bottom*, rings have been lubricated and barrel filled with desired amount of powder.

This applicator is very simple to use, is of rugged construction, has maximum efficiency, and can be used with any preparation. It can be supplied in any desired dimensions, though the size shown is the adult size generally used.

617 Medical Towers (25).

This applicator is manufactured by Scientific Glass Blowing Company, Houston, Texas.

LIPOPROTEINS.—Some gerontologists claim that atherosclerosis is a natural process of aging. The possibility of the occurrence of coronary artery disease at any age, even in childhood, and the failure of finding atherosclerosis in some individuals attaining the age of eighty or more years, leads one to suspect that atherosclerosis is a disease state rather than a natural process. The present popular concept is that it is an alteration of fat metabolism. The plasma lipids in man are made up principally of esters of fatty acids and glycerol, which are the neutral fats or triglycerides, phospholipids, which are fatty acids in combination with phosphorus and nitrogen compounds, cholesterol, and cholesterol combined with fatty acids or cholesterol esters and free fatty acids. These lipids are too insoluble in water to exist in solution in the body fluids and therefore with the exception of fatty acids they are combined with globulin, forming a group of large molecular substances called "lipoproteins."—J. H. Hodges, M.D., Cholesterol and Vascular Disease, *The West Virginia Medical Journal*, October, 1958.

DIAGNOSTIC PROBLEMS

ERYTHREMIA (POLYCYTHEMIA VERA), RADIATION THERAPY, AND LEUKEMIA

Clinical Pathological Conference (PM 1187-57), Oct. 24, 1957, from the Department of Pathology and the Hektoen Institute for Medical Research of Cook County Hospital, Chicago, presented for publication by Daniel S. Kushner, M.D., and Paul B. Szanto, M.D.

Clinical Data

A 37-year-old woman was admitted to Cook County Hospital on July 31, 1957, complaining of shortness of breath, loss of appetite, and a rash. Two weeks before admission, she developed an eruption consisting of large tender "knots" mainly over the knees and anterior aspect of the legs, with only a few on the arms. The lesions progressively increased in size and number for about a week, then gradually regressed. At the height of the eruption, she complained of anorexia, nausea, and night sweats and had a temperature of 100 to 101 F (37.8 to 38.3 C), with one elevation to 103.2 F (39.5 C). She had no chills or joint pains. On the day before entry, she noted increasing substernal pain, aggravated by deep breathing, and a harsh, rasping, nonproductive cough. During the present illness, she also had complained of weakness, dizziness, exertional dyspnea, orthopnea requiring two to three pillows, loss of taste for cigarettes, nocturia (two times), and "reddish" urine. She admitted to ordinarily drinking only an occasional beer.

She had been closely followed in another clinic for six years. In 1950, she inadvertently noted a mass in the left upper abdominal quadrant that was regarded by her physician as an enlarged spleen. In February, 1951, she suffered a fall, and, in the course of examination at the other clinic, splenomegaly (20 cm.) and erythremia (polycythemia vera) were observed.

Basal metabolism and I^{131} uptake were normal. Sternal marrow aspiration revealed cellular marrow, increased megakaryocytes, and erythrocyte-leukocyte ratio of 1:1, normoblastic erythropoiesis, toxic granulopoiesis, moderate increase in histiocytes, and platelet clumps. About 20 phlebotomies were performed between 1951 and 1953. In 1952, radiation therapy to the spleen was followed by some decrease in its size. Subsequently, the extremities were irradiated. For one year, she was given triethylene melamine (TEM). In June, 1954, bone marrow aspiration revealed no spicules and large numbers of megakaryocytes among the fibrous strands, and cortisone was given. TEM was again given from March to November of 1956. An intravenous pyelogram showed a hypoplastic left kidney, compensatory hyperplasia of the right kidney, and splenomegaly. During these six years of clinical observation, the patient had remained entirely free of symptoms. History revealed only tonsillectomy in 1950, and treatment for "pus tubes" in 1943. The patient's father died of diabetes and her mother of hypertension.

Physical examination revealed a thin, young woman, appearing acutely and chronically ill. Her temperature was 101 F (38.3 C), pulse rate 120 per minute and regular, and blood pressure 90/60 mm. Hg. Scattered over the anterior aspect of both legs and the ulnar aspect of the right arm were several deep cutaneous nodules (2 by 2 cm. in diameter), which were indurated and tender but not discolored. The superficial cervical veins were slightly distended. The heart and lungs were normal. The spleen extended four fingerbreadths below the costal margin. The liver edge was just palpable. No other masses were palpated. The abdomen was soft and nontender and intestinal sounds were normal. Rectal, pelvic, and neurological examinations were normal.

Urinalysis was negative. Results of hematological examinations are shown in the table. The blood Kahn test was negative. A roentgenogram of the chest taken July 13, 1957, revealed normal heart and lungs; views of the left shoulder taken Aug. 22 were normal. An electrocardiogram was unremarkable, except for sinus tachycardia. The blood nonprotein nitrogen level was 36 mg. per 100 ml., glucose level 158 mg. per 100 ml., total serum proteins 5.4 Gm. per 100 ml., albumin level 4.4 Gm. per 100 ml., globulin level 1.0 Gm. per 100 ml., gamma globulin level 0.79 Gm. per 100 ml., cholesterol level 78 mg. per 100 ml., and cholesterol esters 39%. Cephalin flocculation was negative, thymol turbidity 4.1 units, icterus index 9 units, alkaline phosphatase level 3.1 Bodansky units, and blood uric acid level 9.1 mg. per 100 ml. A urine culture taken Aug. 1 produced Klebsiella, aerogenes type, sensitive to tetracycline, chloramphenicol, streptomycin, nitrofurantoin, and sulfisoxazole. Agglutinations for typhoid, paratyphoid, and brucella were negative. A

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Dr. Schwartz is Director, Department of Hematology, Cook County Hospital, and Associate Professor of Medicine, Northwestern University Medical School.

blood culture taken Aug. 7 revealed a hemolytic Staphylococcus pyogenes var. albus (coagulase negative). On three subsequent occasions hemolytic Staphylococcus pyogenes var. aureus (coagulase negative) was cultured. The first of these was taken while the patient was receiving tetracycline therapy and the others while she was receiving streptomycin and para-aminosalicylic acid (PAS). The organism was sensitive to penicillin, erythromycin, tetracycline, and chloramphenicol. A direct Coomb's test and lupus erythematosus preparation were negative. Aspirations of sternum and iliac crest were performed Aug. 1, but no marrow elements were obtained. On Aug. 5 a surgical biopsy of the sternum was performed and revealed small clusters of anaplastic cells (stem cells or blasts).

Urinary urobilinogen was still negative. Cortisone therapy (200 mg. a day) was begun on the 10th day, after which the right ankle pains entirely subsided. Again, symptomatic improvement was gratifying, and, for the next 10 days, her temperature remained between 99 and 100 F (37.2 and 37.8 C). A Mantoux skin test (1:1,000) was negative. Therapy with PAS was begun, and streptomycin therapy was continued.

On the 20th day, new, tender, deep, cutaneous nodules appeared. The spleen had enlarged to the iliac crest and extended 8 to 10 fingerbreadths below the costal margin. She began to complain of left shoulder pain, accompanied by tenderness and warmth, and her temperature rose to 103 F (39.4 C). The administration of eight tablets of colchicine

*Hematological Data**

Date	Hemoglobin Level, Gm.	Hemoglobin Level, %	Red Blood Cell Count, per Cu. Mm.	White Blood Cell Count, per Cu. Mm.	Hematocrit Reading, %	Neutrophils, %	Band Forms, %	Basophils, %	Lymphocytes, %	Monocytes, %	Blasts, %	Promyelocytes, %	Myelocytes, %	Metamyelocytes, %	Histiocytes, %
1951†	16.7	...	8,700,000	17,500	51	78	...	...	21	...	...	...	...	...	...
1952	11.7	...	6,600,000	21,600	...	80	7	...	11	2	...	...	...	...	...
1953	13.0	...	6,500,000	10,000	45	...	...	...	...	...	...	...	...	...	...
1954	15.6	...	5,100,000	2,000	51	...	...	...	...	...	...	...	...	...	...
1955	...	...	...	1,600	39	...	...	...	...	...	...	...	...	...	...
2/1/56	...	...	...	8,200	53	...	...	...	...	...	...	...	...	...	...
8/9/56	...	...	...	3,850	34	...	...	...	...	...	...	...	...	...	...
2/2/57	...	...	...	2,500	35	...	...	...	...	...	...	...	...	...	...
6/12/57	...	...	...	3,000	35	...	...	...	...	...	...	...	...	...	...
7/31/57	...	...	2,200,000	...	43	...	...	...	...	...	...	...	...	...	...
8/1/57	...	...	...	4,400	...	13	5	1	38	12	14	7	4	6	...
8/2/57	...	42	2,950,000	3,100	...	...	...	...	...	...	...	...	...	...	...
8/7/57	...	37	3,000,000	4,900	...	19	20	...	17	43	3	4	3	1	...
8/13/57	...	45	3,000,000	16,000	...	9	5	...	28	18	21	8	9	12	...
8/24/57	...	37	2,630,000	14,900	...	15	3	3	28	13	15	11	3	16	3
8/29/57	...	30	2,030,000	40,400	...	4	2	1	32	5	28	13	4	10	1
8/31/57	...	44	3,000,000	...	...	...	...	...	...	...	...	...	...	...	...

* Blood showed anisocytosis, poikilocytosis, hypochromia, microcytosis, polychromatophilia, stippling, few nucleated red blood cells, Doble bodies, burr cells, tear drop cells, and toxicity.
† Platelet count was 340,000 per cubic millimeter and eosinophils 1%.

On the day after admission, the patient complained of severe substernal pain which radiated to the back, accompanied by dyspnea and restlessness. Two blood transfusions produced marked symptomatic improvement. Her temperature, initially 101 F (38.3 C), rose progressively in the first 10 days to 105 F (40.6 C), despite the successive administration of tetracycline, penicillin, and streptomycin. On the seventh day, a chill was followed by a temperature rise to 105 F (40.6 C) and a complaint of severe pain in the right foot. An area of exquisite tenderness, slight swelling, and warmth was noted on the lateral aspect of the foot, beneath, and just posterior to the malleolus. A harsh grade 3 systolic murmur was heard at the base of the heart. No petechiae were seen. Penicillin therapy (1,200,000 units a day) and streptomycin therapy (1 Gm. a day) were continued. The spleen now extended six to seven fingerbreadths below the costal margin. produced dramatic relief of pain. Prednisone, 20 mg. per day, was substituted for cortisone, and the patient was placed on a Sippy regimen. Because of persistence of fever, penicillin therapy was reinstituted (1,200,000 units per day), with apparent response. Consequently, and in view of the repeated isolation of staphylococci from the blood, 20 million units of penicillin were given daily in intravenous infusion. Although three additional blood transfusions and 10 cc. of gamma globulin were given supportively, her temperature rose to levels between 101 and 104 F (38.3 and 40 C); she became increasingly dyspneic and tachypneic and complained of severe splenic pain. Her blood pressure fell to 78/50 mm. Hg, and her pulse rate was 120. The liver extended four to five fingerbreadths below the costal margin. The spleen extended into the pelvis, and epigastric tenderness was noted. The basal cardiac murmur persisted, and P_2 was noted

to be loud and split. A loud to-and-fro friction rub was heard over the liver. Slight ankle edema was present. She was given oxygen and digitalis but died Aug. 31 after six weeks of acute illness.

Clinical Discussion

Dr. Steven O. Schwartz: The problem for discussion is that of a 37-year-old woman with a six-year history of illness, beginning with an asymptomatic

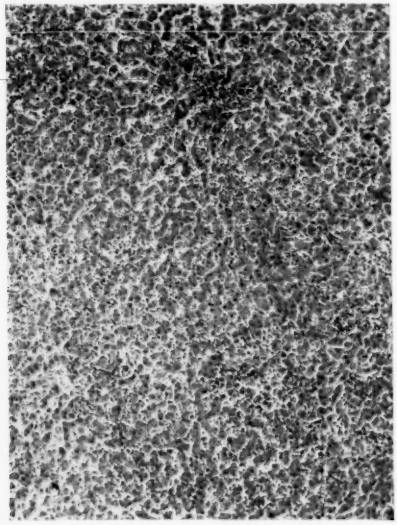

Fig. 1.—Section of liver showing accumulation of mononuclear cells in the sinusoids. Cell types at this magnification cannot be identified.

splenomegaly and erythremia, who was vigorously treated and whose course terminated with six weeks of acute illness, characterized by an erythema nodosum, fever, sweats, arthritis, hyperuricemia, severe anemia, cardiac murmurs, staphylococcemia, pericarditis, cardiac failure, and invasion of the blood by primitive cells. The question is not why this patient died but rather why she developed an acute leukemia and what the preexisting disease was for which she was so extensively treated.

To begin with, one is reluctant to accept the diagnosis of a polycythemia vera in a 30-year-old woman, even though she had a splenomegaly and erythremia, because this is not a disease of the young, but usually of older persons. One then considers other possible bases for erythremia and splenomegaly. First, there is tuberculosis of the spleen, as the consequence of hematogenous dissemination. Against this are the negative chest roentgenogram and her failure to respond to rather vigorous antituberculous therapy. She also had a negative tuberculin skin test. Admittedly, this was done only in a 1:1,000 dilution and, therefore, some might question its validity, and one must also recognize the possibility of anergy in miliary tuberculosis. Finally, in the repeated studies, there were no radiologically demonstrable calcifications in the spleen. On the basis of these factors, it is unlikely that she had tuberculosis of the spleen.

The second possibility is that we are dealing with a myelofibrosis and a compensatory metaplasia in the spleen and erythremia, but the fact that in 1951 she had a normal marrow, with normal myelocyte production, excludes this diagnosis. Therefore, we must conclude from the evidence presented that her original disease, in 1950, was indeed a polycythemia vera, rather early and well compensated. It should again be emphasized that at that point diligent attempts should have been, and probably were, made to rule out the possibility that this was a primary tuberculosis of the spleen. The question next arises as to why this patient was so energetically treated.

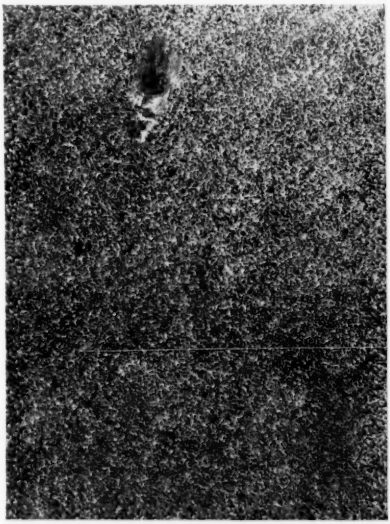

Fig. 2.—Section of spleen showing replacement of splenic parenchyma by fairly uniform type of cells. Megakaryocytes are scattered throughout.

At no time did she have symptoms. Certainly, to give such intensive x-ray and TEM therapy at the age of 30 as to produce profound leukopenia which lasted over the period from 1954 to 1957 was hardly justifiable, regardless of one's therapeutic enthusiasm. Nonetheless, in spite of the enlarged spleen, the patient apparently got along fairly well until 1957, when she developed an acute leukemia.

There are a number of theoretical explanations but no factual explanations. Therefore, we must resort entirely to hypothesis. The first and the simplest is to say that this was a polycythemia vera which developed into leukemia after six or seven years. There is a popular misconception that 10% of patients with polycythemia develop leukemia. If, however, one studies the literature carefully, one finds that patients with polycythemia, who eventually develop leukemia, have at some time been treated with one form or another of radiation therapy. Even more interestingly, with orthodox x-ray therapy, it takes about five years for the development of leukemia, and usually this is a chronic rather than an acute leukemia. This record has been improved on, since it is now possible to produce acute leukemia in two years. The minority opinion, therefore, in this controversial matter, is that x-ray treatment in polycythemia vera is not only not the treatment of choice but is definitely contraindicated.

If one accepts the thesis that this patient had polycythemia vera and, in some way related to intensive and prolonged radiation therapy, subsequently developed leukemia, we must deal still with the question of why the leukemia developed. The TEM might also have played some role in its development.

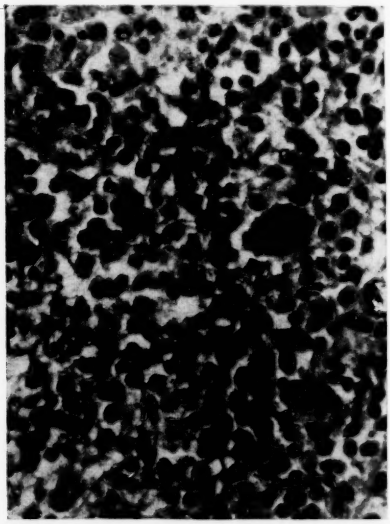

Fig. 3.—Higher magnification. Many cells belong to myeloid series—myeloblasts and myelocytes.

If one does not believe that this patient had a preexisting disease which predisposed her to develop leukemia, then one must find still another explanation. The concept of the myeloproliferative disease syndromes, currently in vogue, permits one to accept an initial proliferation of the erythrocytes, later proliferation of fibrous tissue elements, and eventually proliferation of the white blood cells. One could also look on x-rays as carcinogenic and think of the leukemia in this patient as having been produced by the x-rays. One might assume, however, that the roentgen radiation simply predisposes these patients to the development of leukemia. This seems to us the most interesting of all the hypotheses. We know that leukemia develops much more frequently in those who have been exposed extensively to roentgen rays than in the whole population. Unless one thinks of x-rays as being carcinogenic, one must assume that the x-rays simply make these people more susceptible to leukemia.

Fig. 4.—Section of bone marrow showing fatty marrow of femoral diaphysis replaced by very cellular erythromyelopoietic tissue. Many cells are myeloblasts and myelocytes. Smaller cells with black nuclei are normoblasts.

If it makes them more susceptible, then the question is, what is leukemia? How does this fit into the whole concept of leukemia? Leukemia is nothing more than a proliferation of the various cells normally present in the body, either as a result of the carcinogen effect of x-ray producing theis myeloproliferative disease, or, it may be a proliferative response to some insult to which the x-ray radiation has made the organ system susceptible. I like to think that this is what happened in this patient. Her resistance in the course of years, both as a

result of the x-ray and the TEM therapy, was gradually reduced. The fact that she appeared chronically ill implies that before the clinical manifestations became obvious and before she came under observation, she had already been ill for some time. Then, having been made susceptible to the

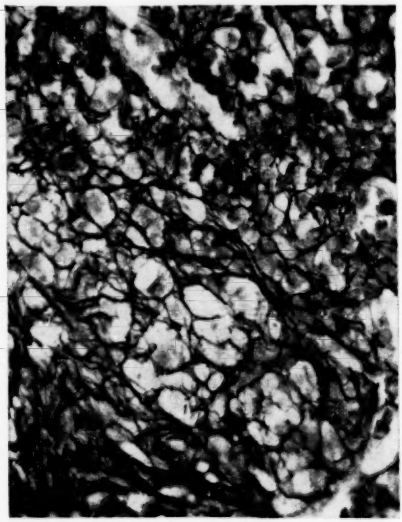

Fig. 5.—Section of bone marrow showing numerous reticulum fibers and collagen fibers.

development of leukemia, she developed it terminally as a result of her granulocytopenia. She certainly became susceptible to gross bacterial infections. She developed a bacteremia as evidenced by both the urine and blood cultures. I would be surprised if she did not, in addition, have liver abscesses. She died in cardiac failure, probably with pulmonary edema. One interesting point is that in 1951, the basal metabolism and the I^{131} uptake were normal, but at the time we saw her, she had weight loss, increased oxygen demand, and a high blood uric acid level, indicative of an increased metabolic demand and rapid nucleoprotein turnover.

Dr. S. Howard Armstrong, Jr.: Why did this patient die? Her hematological abnormalities hardly seem sufficient to explain the precise cause of death.

Dr. Schwartz: I think she died of cardiac failure and pulmonary edema, which I assume to be on the basis of myocardial failure secondary to the long duration of the illness, the moderately severe anemia, the increased metabolic demands of the underlying leukemia, and the terminal acute sepsis.

Dr. Armstrong: Could anything have been responsible other than what was defined bacteriologically? With regard to the isolation of staphylococci from the blood, in light of the skin lesions so suggestive of erythema nodosum, we can make three kinds of divisions. The fulminant coagulase-positive yellow staphylococci cause petechiae. These can go on to become white centered and resemble pyoderma, and the coagulase-negative staphylococci, which rarely cause septicemia, can produce a sort of granular erythema nodosum type of lesion from which staphylococci can be cultured early. Also, the hypoplastic kidney on one side, with a big kidney on the other, is a common observation in pyelonephritis. One must still dispose of the problem of a leukemoid response to severe infection.

Dr. Schwartz: The thing that prejudiced us against the purely bacteriological components of this case is that one of our group who saw the patient noted that she did not appear toxic, in spite of the severity of her illness. This suggested a terminal leukemia rather than infection.

Dr. Armstrong: This is important.

Fig. 6.—Section of myocardium showing infiltration by mononuclear cells belonging to myeloid series.

Dr. Harold Schoolman: What is the relationship of myelofibrosis to leukemia, and, could this patient have had this leukemia seven years before it became manifest?

Dr. Schwartz: With regard to the question of whether myelofibrosis antedates leukemia, in this patient the myelofibrosis was demonstrated first, so

the answer is, yes, it can and did. This, however, must be modified by an explanation of what causes myelofibrosis, since we often see an acute leukemia in the so-called aplastic phase, which is similar to myelofibrosis. The second question is, could she have had the leukemia seven years ago. There is no evidence that she did. In the protocol, the marrow was described seven years ago as having a 1:1 ratio with no abnormal granulopoiesis, and I cannot interpret that, even in retrospect, as leukemia.

Question: Would it be pertinent that this patient complained of ankle pain and swelling and developed an area of exquisite tenderness and pain on the lateral aspect of the foot, beneath the lateral malleolus, and then responded dramatically to colchicine?

Dr. Schwartz: With a 9.1 mg. uric acid and a dramatic response to colchicine, in spite of the fact that this was in a woman, and in spite of the fact that she was 37 years old, I would have no quarrel with a diagnosis of secondary gout.

Clinical Diagnosis.—The final clinical diagnosis was acute granulocytic leukemia developing as a result of radiotherapy of a previous polycythemia vera and terminal staphylococcal pyelonephritis and septicemia.

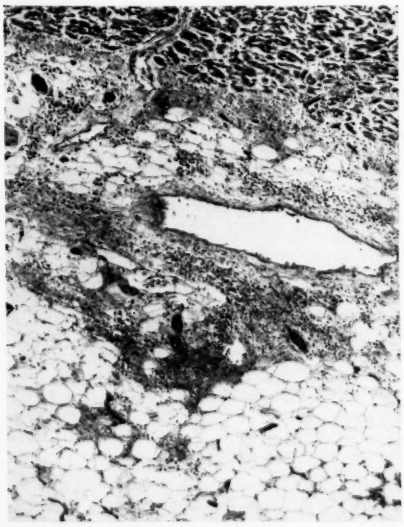

Fig. 7.—Section of subepicardial fat tissue showing infiltration by cells belonging to myeloid series.

Pathological Data

Dr. Paul B. Szanto: The body was that of a well-developed, somewhat emaciated woman. The pituitary was enlarged, as seen in multiparous women, due to increase in chromophobic and sparsely eosinophilic granulated cells of the anterior lobe. A moderately sized goiter (40 Gm.) was present. A mild peptic esophagitis was present which may have been responsible for the epigastric symptoms and signs. Corresponding with the history of "pus tubes,"

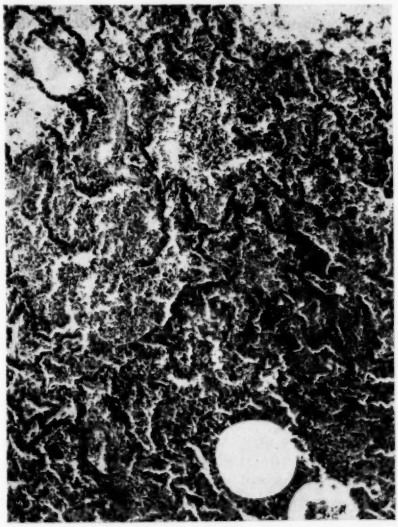

Fig. 8.—Section of lung; many cellular elements in alveoli are identified as myeloblasts and myelocytes.

there was a bilateral hydrosalpinx. A confluent bronchopneumonia involved the lower lobes of both lungs. All cardiac chambers were dilated (weight 350 Gm.). Subepicardial hemorrhages were noted. Microscopically, the myocardium and epicardium showed cellular infiltration. The central nervous system showed some degenerative changes in the granular cell layer of the cerebellum, as seen occasionally in chronic alcoholism. The left kidney was hypoplastic and showed changes of a chronic pyelonephritis. The right kidney showed compensatory hyperplasia. Chronic pyelonephritis is frequently superimposed on a hypoplastic kidney.

The liver was enlarged (1,950 Gm.), and, on section, the lobular architecture was not discernible. Microscopically, the portal fields were moderately enlarged and cellular. The sinusoids were extensively infiltrated by mononuclear cells (fig. 1). Megakaryocytes were also prominent. Many of the mononuclear cells were myeloblasts and myelocytes. The hepatic changes alone permit the diagnosis of a recent exacerbation of a chronic granulocytic leukemia.

The spleen was large and firm (1,800 Gm.). The splenic tissue presented a homogenous appearance, and the follicles were obscured. In acute leukemia, the size of the spleen is usually around 300 to 400 Gm. In erythremia, as this case was originally diagnosed, the weight of the spleen is usually between 300 and 500 Gm. The large size of this spleen would suggest either agnogenic myeloid metaplasia or chronic granulocytic leukemia. Histologically, the architecture was obliterated. The Malpighian corpuscles were absent. This is important, because the absence of the follicles rules out the possibility of agnogenic myeloid metaplasia. This diagnosis had to be considered because erythremia may occur in the early phase of agnogenic metaplasia. In this case, microscopically, the splenic tissue was replaced by cells of fairly uniform cell types (fig. 2), myeloblasts and myelocytes intermingled with megakaryocytes (fig. 3). All lymph nodes were moderately enlarged, discreet, and on cut section gray-white and bulging above the level of the capsule. Microscopically, the normal architecture was obscured due to infiltration or replacement of the normal lymphoid tissue by cells of the myeloid series.

The bone marrow was very cellular (fig. 4), including the fatty marrow, which was replaced chiefly by myeloblasts and myelocytes, with distinct scattered megakaryocytes. In some areas of the bone marrow, just as in the biopsy specimen, fibrous replacement was seen. In these areas, numerous argentophilic reticulum fibers and collagen fibers were seen (fig. 5). The diagnosis of focal myelofibrosis of the bone marrow is confirmed. Iron pigment was completely absent in the bone marrow, liver, spleen, and lymph nodes. Some of the other organs also showed myeloid infiltrations. The spinal ganglia were infiltrated by cells of the myeloid series. The colon showed superficial ulcers with infiltration of the submucosa by cells belonging to the myeloid series, especially myeloblasts and myelocytes.

Returning to the heart, the infiltration of the myocardium (fig. 6) and subepicardial fat tissue (fig. 7) consisted of myeloblasts and myelocytes; thus, a leukemic infiltration of the myocardium resulted in cardiac dilatation. A closer examination of the lung revealed that most of the cells in the alveoli were myeloblasts and myelocytes (fig. 8).

Pathological Diagnosis.—The pathological diagnosis was chronic granulocytic leukemia with recent exacerbation, leukemic infiltrations of lymph nodes, spleen, liver, colon, myocardium, and lung, and focal myelofibrosis of bone marrow; bilateral confluent bronchopneumonia, lower lobes; peptic esophagitis; chronic pyelonephritis of the left kidney, and compensatory hyperplasia of the right kidney.

Comment

Dr. Szanto: Myelofibrosis or "myelophthisic" states may occur secondary to (1) irradiation, (2) chronic benzol poisoning, (3) carcinomatous metastasis leading to a desmoplastic reaction, (4) aplastic anemia, and (5) unknown causes. Myelofibrosis of any cause may lead to myeloid metaplasia in the various organs, especially the spleen. The so-called agnogenic myeloid metaplasia (chronic nonleukemic myelosis)[1] is characterized by a progressive hepatosplenomegaly, with preservation of the Malpighian corpuscles, and it may or may not be associated with myelofibrosis. As mentioned above, in this case, the Malpighian corpuscles were absent, and the architecture of the spleen was completely obliterated. It should be pointed out that in our experience most of the cases diagnosed as agnogenic myeloid metaplasia are atypical forms of chronic granulocytic leukemia. In this case, none of the causes enumerated above were present to explain the myelofibrosis.

This 37-year-old woman developed clinical and hematological findings, interpreted six years prior to her death as erythremia. Although the possibility exists that polycythemic blood findings (erythrocytosis, but no true erythremia) may develop in the early phase of an agnogenic metaplasia, a review of the original symptoms makes the diagnosis of erythremia (polycythemia vera) acceptable. In the subsequent two years after the diagnosis of polycythemia vera was made, the patient received energetic treatment consisting of numerous phlebotomies and radiation. Later she developed moderate anemia, leukopenia, and a hypocellular bone marrow, findings which may reflect the myelofibrotic changes in the bone marrow. In the last months of her life, she developed an acute exacerbation of a chronic granulocytic leukemia.[2] We agree that the joint pains were manifestations of a secondary gout as occurs in leukemia. The marked orthopnea may be related to the extensive leukemic infiltration of the lungs. Myelofibrosis and myelosclerosis may develop in the course of leukemia. In leukemia, as well as in erythremia,[3] the leukemic process may lead to an increased activity of the fibroblasts and/or osteoblasts, or it may simulate the differentiation of the mesenchymal cells of the bone marrow into fibroblasts or osteoblasts.

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3. Wasserman, L. R.: Polycythemia Vera—Its Course and Treatment: Relation to Myeloid Metaplasia and Leukemia, Bull. New York Acad. Med. **30:**343-375 (May) 1954.

"All the comforts of home" is no cliché in a modern nursing home where couples may share their declining years in comfortable surroundings. Medical supervision and skilled nursing care play a key role here (see "Nobody Calls This an Institution," page 146.

MEDICINE AT WORK

- *Nursing Homes Roundup*
- *Secrets Not to Keep*
- *War on Staphylococcus*
- *Prescription Against Quackery*
- *'Village' for Oldsters*
- *Quotes from Minneapolis*
- *Where the Aged Don't Worry*

Sunrise and Sunset

Concern for infants matched concern for oldsters in the science-socioeconomics area which confronted the A. M. A. House of Delegates in Minneapolis last month. This is what the Committee on Maternal and Child Care announced as a goal:

The objective of perinatal mortality and morbidity studies is to improve the production of normal human beings. The elimination of deaths and damage during the process of reproduction is the ideal for which we should strive.

And this is from Governor Orville L. Freeman of Minnesota:

Can you help us to find a way to apply the voluntary health insurance principle to elderly and retired people? Can you help us to develop a program, that is within our means, to provide the kind of preventive care and attention that will make the sunset years healthier and happier? The people feel this need and when they feel it badly enough, they demand that it be met. The people then say, "there ought to be a law." Yet the best solution is seldom reached in an atmosphere of urgent need or bitter controversy.

On both of these challenges, the House took definitive action, adopting the Committee report as well as a far-seeing program for the aged.

For other selected quotes from the Clinical Meeting in Minneapolis Dec. 2 to 4, see page 150 of this section. A series of Medicine at Work reports and photos relating to facilities for the aged begins on this page.

What Is a Nursing Home?

Society Searches for an Answer as Facilities for the Aged Boom

"The term 'nursing home' has been used so indiscriminately that it has almost ceased to have any meaning." This statement, made a few years back by the director of an agency for the chronically ill, outlines the situation involving nursing homes today which is ambiguous: people talk a good deal about nursing homes, but often they are not talking about the same thing.

The Public Health Service, in a monograph called "Nursing Homes, Their Patients, and Their Care," underlines this national confusion. It states:

As a relatively new type of facility, the nursing home is not yet clearly conceived and understood. Like most newly emerging social institutions, it was not established full-blown and definitive; it has found its way gradually, hesitantly, and to a great extent, expediently. What it offers therefore is not necessarily always the professionally appropriate answers to the problems it attempts to meet, but rather responses dictated by immediate practicalities. It is not a homogenous type of institution; it means different things in different localities or to different people.

But lack of a proper definition has done little to dampen the growth of nursing homes in this country. Though their number was insignificant in the Thirties, a detailed survey made in 1953-'54 disclosed a national total of 25,000 establishments that qualified as nursing homes under the generous working definitions used in the PHS study.

Whatever their other variations, those homes surveyed by PHS were in agreement on one thing at least: they catered almost exclusively to the needs of the aged. Figures show the average age of the patients to be 80. Fewer than one-tenth of the residents of these homes are less than 65. As might be expected in this age grouping, women outnumber the men two to one.

Medical or Social Need?

Nursing homes are an outgrowth of our modern society with its highly complex social, medical, and economic structure. They have been created to fill a need that may be almost as much social as medical. Their func-

tion in the modern scheme appears to be poorly understood by the public.

These homes occupy a position in the medical care spectrum between the home for the aged and the chronic disease hospital, with overlaps at each end. Some have highly organized medical direction and offer housing almost as an adjunct. Many others are primarily shelters that operate without even the benefit of a trained practical nurse. They come in all sizes, too. While more than four-fifths of the 25,000 listed by PHS were proprietary, these accounted for less than half the total number of beds. The other half were in homes operated by voluntary organizations or governmental units.

Such a burgeoning area of medical care could not be long ignored by those interested in the health of the nation's oldsters. Attempts to develop standards for such homes are being or have been made by the American Medical Association, the American Hospital Association, the Public Health Service, and the American Nursing Home Association. Last November, the AHA announced it was prepared to inaugurate a program "to list inpatient care institutions other than hospitals as nursing homes." An attempt to correlate the resources of the principal purveyors of health care for the elderly has been undertaken by the Joint Council to Improve the Health Care of the Aged. Formed last year, the group's membership includes representatives of the A. M. A., ANHA, AHA, and the American Dental Association. They have labored tirelessly to bring about a solution to this broad and complex problem.

Definition by Function

Although their practices differ widely, nursing homes have been categorized by the Public Health Service in three classifications—one with two subdivisions:

Skilled Nursing Homes. Those capable of offering procedures, employed in caring for the sick, which require some technical nursing skill beyond that which the untrained person can administer.

Personal Care Homes. Those offering primarily such personal services as help in walking, getting in and out of bed, bathing, diet supervision, and aid with self-administered medications.

Sheltered Homes. Those offering room, board, custodial services, laundry, and minor personal services.

It soon became apparent that personal care homes were of two distinct types: those that offered personal care only, and those that had the personnel and equipment to offer skilled nursing services to a portion of the residents.

A current effort by the Public Health Service to identify various types of facilities by means of a numbering system came in for sharp discussion last month when the A. M. A. was host to officials of PHS, AHA, and ANHA at a meeting in Chicago. Purpose of the proposed numbered categorization would be to aid states' attempts at licensure.

In its current effort to study and develop data on nursing homes, the A. M. A.'s Committee on Medical and Related Facilities of the Council on Medical Service sent inspection teams to 35 geographically separated nursing homes last summer. Places chosen were considered to be among the nation's best.

For examples of two of the 35, see "Village for the Aged" on Page 149 and "Nobody Calls This an Institution" on Page 146

Preliminary reports of inspection teams indicated a variety of conditions in these homes. One stated: "There have been a few homes where the medical staff set-up, on paper, looked like the answer to a patient's prayer. Then you find that the medical director is in, perhaps, at the most once a week, and that the majority of medical supervision is handled by nurses."

Other inspections in the series pointed up a certain lack of agreement as to what constitutes proper social and rehabilitative programming in these homes. In some, the visitors found physical and

Yellow-Page Puzzle

The pages of a classified telephone directory in just one U.S. metropolis lists 149 establishments under the heading "Nursing Homes," yet the advertisements for these same homes indicate how their functions vary.

One, calling itself a convalescent home, offers "hospital care." Another, managed by a practical nurse, also caters to convalescents—and the elderly retired. Some advertise that they accept "mental cases," but they usually stress the adjective "mild." Others exclude "mental cases or alcoholics.'

The nursing home classification also states: (see also Sanitariums). A look at the listings for sanitariums shows duplicate listings for many of the establishments also classified as nursing homes.

The phone book of another large city lists a similar array under the catch-all title of nursing homes, yet one of its offerings advertises itself as a "hotel for senior citizens—not a convalescent home." That place does, however, have "complete medical services available."

occupational therapy programs going full tilt with the approval of the residents. In others, such services were largely unused because the staff had been unable to interest the patients in participation. Indeed, in one home, the administrator questioned the value of occupational therapy as a morale builder, and avoided it as a matter of policy.

Is Money the Root?

Money—or, to be more accurate, its absence—often lies behind some of the more obvious faults of nursing homes. Dr. Willard Wright, chairman of the A. M. A. Committee on Medical and Related Facilities, says: "Increasing numbers of persons are dependent on various forms of governmental assistance. Frequently it is in this area that operators of nursing homes find themselves held down to such low income that they are unable to provide the best type of services."

This problem is greatest in those states where an indigent care program is not available. And yet, some homes—such as Mary Manning Walsh in New York, and Good Samaritan Village in Hastings, Neb. —operate successfully in spite of this handicap.

Medical care in the homes visited by the A. M. A. teams varied widely, yet staff men making the inspections found that the effectiveness of such care and supervision depended far more on the interest and effort of those taking part than on the plan itself. They found that many of the larger and newer homes had one or more full or part-time staff physicians who handled almost all the day-to-day medical care in the home, as well as responsibility for general medical policies. The other extreme was represented by small homes which had no staff physician, but engaged in various kinds of working relationships with local doctors, many of whom had their own patients in the home.

"In these latter cases," an interim A. M. A. report states, "one of the local physicians often acts as a confidant or advisor to the nursing home administrator on general medical problems. This type of arrangement is usually as informal as picking up a telephone, but depending on the attitude of the physician and administrator, has proved completely adequate for insuring good medical policies."

The physical plants of these homes vary almost as widely as do the administrative policies that guide them. Many of the smaller ones inhabit large homes dating back to an earlier era which offer stately surroundings often ill-suited to the needs they are expected to satisfy. With less than half their patients ambulatory, and a large proportion mentally disoriented at least part of the time, nursing homes have some important safety problems to consider and overcome. They are not always successful, as was violently illustrated a few years ago when 70 patients were incinerated in a Midwestern home as fire razed their quarters.

Other homes have been formed in more suitable, though unorthodox, facilities. Some have been constructed for the express purpose of housing a nursing home, but these appear to be the fortunate minority. More often they occupy quarters constructed for purposes now outdated: a school, a housing project, a former hospital.

Chairman of the A. M. A. Committee on Medical and Related Facilities of the Council on Medical Service is Dr. Willard Wright of Williston, N. D. Other members are Drs. William F. Costello of Dover, N. J.; Robert L. Novy of Detroit; David Henry Poer of Atlanta; W. C. Stover of Boonville, Ind.; Walter E. Vest of Huntington, W. Va.; and John M. Rumsey of San Diego, Calif. Dr. Edward C. Rosenow of Los Angeles is a consultant to the Committee. Staff Secretary is Mr. George W. Cooley.

Interest Quickening

Interest in the field of aging is on the upswing. Not only are nursing homes and similar facilities burgeoning, but public and professional concern with the problems of the elderly becomes more apparent daily. Within the past decade, giant strides have been made in this field. All states now have licensure laws covering nursing homes. The ANHA (grown to 4,500 members from a mere handful in 1954) works valiantly with other interested health groups to develop standards. In addition, the ANHA spends much of its time on educational programs for home operators.

The answer to all of this renewed interest is probably manifold: The obvious reason lies in the actuarial tables which show ever-increasing numbers reaching and surpassing the historic three-score-and-ten. A less obvious answer, but perhaps an even more pertinent one, was advanced last year by Dr. Cecil Wittson, a psychiatrist who is a member of the A. M. A. Committee on Aging. Speaking in Chicago before the A. M. A. Planning Conference on Aging, Dr. Wittson told the assembled physicians:

"Careful research over the past 2,000 years has finally established that senility has an incidence of 100 per cent among living populations. Geriattrition is the common fate of man. For once, the healthy future you are attempting to guarantee is not the other fellow's—it is your own."

Being dependent on a wheelchair doesn't mean inactivity for residents of the Mary Manning Walsh nursing home. Games and sports add interest and therapeutic opportunities to the home's daily schedule.

Nobody Calls This an Institution

Folks at Mary Manning Walsh Home Haven't Time to Worry About Old Age

There was concern, but no panic, when one of the aged male residents of the Mary Manning Walsh home on Manhattan's 59th Street failed to show up for lunch. Police were alerted and the Sisters scoured the neighborhood, but, even at dinner time, no trace could be found of the errant guest. It was late in the evening when he finally returned, tired but happy after a long day—spent at a Long Island race track.

In many nursing homes, the incident might have been the signal for a tightening of restrictions on the home's residents, but at Mary Manning Walsh, operated by the Carmelite Sisters, Mother Bernadette views such occurrences as a natural by-product of a policy that encourages all the activity, interests, and cosmopolitanism any resident finds himself capable of.

In a "constantly adapting" policy of administration, Mother Bernadette has come up with some happy solutions for some old problems:

For a retired milliner finding it difficult to adjust to the new life—a basement hat shop that serves the dual purpose of keeping her happily busy, and providing new bonnets for the home's feminine residents.

For those liking a nip or two but finding the local tavern too much of a good thing—the Emerald Room, a bar, complete with a red-jacketed, brass-buttoned bartender, that opens daily at 4 p. m. and serves cocktails for a "donation," a system which obviates the need for a liquor license.

For residents who want to feel they have a part in the operating decisions of the home—a resident council that weighs submitted ideas carefully, transmitting the best to a usually amenable administrator.

Hotel for the Elderly

Although Mary Manning Walsh home is an "institution" by definition, it has few of the undesirable attributes commonly associated with the term. A home for more than 300 persons, chiefly women, it occupies three interconnected buildings that formerly housed the New York Orthopedic Hospital. Operated on a nonprofit basis by the Roman Catholic Archdiocese of New York, the home offers several grades of care for the aged on a hotel-like basis. Open to all, regardless of race or religion, it is governed by a nine-man board that includes physicians, businessmen, lawyers, a Cardinal, and others. Couples, as well as individuals, are accepted. Female residents outnumber the males by about 5 to 1.

Medicine's role in the seven year history of Mary Manning Walsh home has been a constant one. Indeed, its medical problems were carefully considered by physicians before the home was opened. Dr. Howard Rusk, director of the Institute of Physical Medicine and Rehabilitation of New York University–Bellevue Medical Center, provided guidance in the early days and has continued his interest as a member of the home's board of directors. Dr. John F. Maloney, medical director for the home, supervises all medical care and matters of medical policy. Other staff physicians include Drs. Michael Dasco, Ann Maloney, and John Sokolow, who are retained on a part-time, paid basis. In addition, a number of the city's medical specialists act as consultants when needed.

The resident arrives at the home with a medical

If Mary Manning Walsh home had a formal slogan, it would probably be "The Residents Come First." Facilities and programs are in a constant state of flux as Mother Bernadette works to better her home's services. She says:

"We don't want to modify the living habits of the residents any more than is absolutely necessary. We try to make Mary Manning Walsh as much like the homes they came from as possible. If they've been used to a drink before dinner, a snack between meals, or smoking a pipe, we want them to continue to do so here. Our convenience is secondary to their happiness."

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history and referral sheet filled out by his physician. Within 24 hours, he is given a physical examination by a member of the medical staff. Medical care during residence is based on the individual's condition, but the emphasis is on rehabilitative procedures for those suffering from illness or disability. Residents may have their own physicians, but staff doctors make a daily check on the condition of those needing skilled nursing care.

No Time for Self-Pity

The range of activities open to residents is extensive. In addition to the usual therapeutic arts and crafts, a resident may help plan and write a bimonthy newspaper, take photographs, act in or direct one of the many plays or shows, play the piano, sing with a choral group, take a course in music appreciation (or teach it), go for a boat ride around Manhattan, spend a few hours on a picnic, get a permanent or a haircut, entertain visitors in the snack bar, play games, or just read, chat, or meditate as the spirit moves.

Parties and special occasions are celebrated in constant succession at Mary Manning Walsh. Wedding anniversaries, birthdays, and legal and religious holidays all come in for special attention. In the summer, the buildings' balconies and roofs are used for exercise and entertainment, and, in cooler weather, the home's auditorium often is the scene for shows put on by visiting entertainers, many of them performers at one of the city's larger night clubs whose owner is interested in the home.

The majority of the home's residents are in their eighties. Most of them suffer from some handicap, many are bedfast or in wheelchairs. Yet some of them manage a surprising amount of activity:

—One woman won quite a TV following on a show featuring the aged.

—A male member of the home used his age to good advantage when he appeared as the model, complete with tattoo, in a national advertising campaign for a cigarette company.

—An architect, living in the home with his wife, still works as a consultant in his profession.

Beds and Wheelchairs, Too

While the more active residents provide for their own interests, the less fortunate are not forgotten. Bedfast patients, in addition to expert nursing care, are given small attentions too. A supply of pretty gowns and bedjackets are liberally used, and shampoos and hair grooming are offered as needed. For those confined to wheelchairs, a variety of therapeutic activities is maintained, even such unlikely ones as bowling and badminton.

Some of the home's residents are dependent on public assistance; others are provided for through their own resources or those of relatives. The administrator says the home is self-sustaining, partly due to the fact that many of the staff are members of the religious order. Groups of nursing aides are assigned to the home for two-month training periods.

Mary Manning Walsh home gives every appearance of being almost an unqualified success—and appearances, in this case, are not deceiving if you listen to one of the home's first residents. A retired physician, Dr. Francis A. Schneider, on the occasion of the home's fifth anniversary, wrote:

"Five years and three months have rushed by . . . never wondering what to do with ourselves, never lonesome, but always occupied wishing the day would take on additional hours. My roommate (alias wife) has so many interests that I fear our relationship might be reduced before long to a mere bowing acquaintance from a distance. As for myself, I have widened my horizon in knowledge, hobbies and experience to such an extent that an enumeration of them before our entrance [to the home] would have sounded ludicrous."

No Miracle on 59th Street—
Just a happy home amid tenements

Routine Medical—
One of many check-ups

On this and the preceding page are scenes from the Mary Manning Walsh home on 59th street in Manhattan. While medical care is a key factor in this nursing home that "nobody calls an institution," a myriad of other important aspects are called into play—a millinery shop, a bar, bowling, arts and crafts.

Easy Does It—
Rehabilitation in action

How Perky—
The millinery shop

Keeping Busy—
Everybody works at something

An Aperitif—
The bartender lives here, too

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'Village' for the Aged

Nebraska Unit Emphasizes Medical Care at Every Level of Need

People never grew old in Sir James M. Barrie's "land of never-never," and it might be argued that this has practical as well as theoretical advantages. For one thing, its citizens did not need to worry about such matters as pensions and social security.

But in Nebraska—just as in the rest of the world—aging has its problems, and it is here that a "village" devoted to the needs of the elderly is growing. Opened to residents only eight months ago, it had nearly 200 admissions last year.

Good Samaritan Village is geared to the requirements of the aged whether they may be retired couples able to care for themselves or bedridden patients without home or family. Sponsored and originally financed by the Good Samaritan Society, a Lutheran church-related group which operates 60 nursing and old age homes, the Village was founded in a wartime housing development known as Spencer Park, an outlying section of Hastings. Although a community unit in its own right, the "village" has no civic government of its own.

It was established in 1957 with the purchase of about half of the project's 850 apartments. An option was taken on the other half, and the Society is currently awaiting a decision on its application for a $425,000 FHA-insured loan. Streets and sidewalks are paved, and all apartments are equipped with gas radiant heating units and water heaters.

Rev. William Goldbeck, an ordained Lutheran minister, became administrator of the 80-acre Village after serving as chaplain at the nearby Hastings State Hospital. He is aided by an advisory committee made up of the business and professional leaders of Hastings. Other volunteer groups help out with recreational ventures.

Plan for Medical Care

A local physician interested in geriatrics, Dr. Gerald Kuehn, acts as medical director of the rest home and infirmary. Recommended by the Adams County Medical Society, he supervises the over-all medical program, acts as physician to those who have none, and is available in emergencies. Many residents make their own arrangements with private physicians, as do some of the infirmary patients.

Hospital care is available to Good Samaritan Village residents at the 138-bed general hospital in Hastings, a short drive away. Laboratory work is currently done through outside facilities, but an enlarged infirmary now in the planning stage will include a laboratory as well as facilities for oxygen, basal metabolism rate equipment, electrocardiogram, x-ray, and sterilization.

The Village is designed to operate on a non-profit, self-sustaining basis offering "security, Christian care, and companionship" for those of normal retiring age or who for other reasons must limit their activities. Five levels of care are available:

—One to three-bedroom apartments for couples or individuals who are capable of caring for themselves, and who seek only the companionship of others of their age group.

—Similar apartments for those who can maintain their own households with assistance from a "house visitor" who will come each day to help with household duties and meal planning.

—The same living arrangements as above, but with provision for one or more meals in a central dining room.

—A rest home providing personal care under medical supervision for those who need help with feeding, dressing, walking, and similar activities.

—An infirmary section of the rest home for those in need of nursing care and medical supervision.

Apartments consist of a kitchen, living room, and from one to three bedrooms each. Monthly rental is $25, $30, or $35—depending on the number of bedrooms. Cost of gas and electricity is extra. For those found to require it, the "house visitor" will drop in at no extra charge. There is an extra cost for meals eaten in the central dining room.

Care in the rest home includes meals, laundry, and room service. For the patient up and about, the cost is $85 to $95 a month. Cost for the person in a wheelchair or walker is $100 to $125. Bed care in the infirmary is available for $125 to $150 a month. An expected innovation will be suites for couples in the rest home, each with a private bath.

Population Possibilities

First occupants of the Village moved in last summer. At last report, only a handful of the apartments had been rented, but the existing infirmary was filled to its capacity of 11 patients. Additional construction underway will increase capacity to 52 this spring. The rest home is also in its infancy but will be able to accept 92 residents on completion. Eventual population of the Village may reach 800 or more, if all available housing is used. Residents furnish their own apartments—a point which, it is hoped, will help to make them feel at home.

Plans for the future at Good Samaritan Village are hopefully farsighted. Additions to the physical plant will include a shopping center, chapel, recreation center, park, greenhouse, library, and hobby shop. Due for increasing emphasis are social services and rehabilitation programs.

While the land of Peter Pan has not lost its appeal to our imaginations, it is well to view aging in a more pragmatic light. Answers to the problem of caring for the elderly are eagerly sought today, and Good Samaritan Village is convinced it has one of the better solutions.

They Said It at Minneapolis . . .

Some significant comments reported "on the record" at the 12th Clinical Meeting last month:

Unfortunately, many people who habitually advocate government solutions to health problems do so on the basis of political expediency. Some of them, including well-intentioned physicians, support such programs because of the motives and objectives involved, but they choose to ignore or minimize the great dangers inherent in the means. As a result the medical profession frequently is forced into opposing legislation which has a worthy goal, but which offers numerous pitfalls for both medicine and the public.

We should make our views known—in community affairs, on national issues, on any and all questions of the day. There is a direct relationship between the future of individualism and the ultimate fate of the medical profession.

In our relations with third parties we cannot deny the validity of criticism. We should welcome it, study it and learn from it. . . .We also should appraise some of our own programs—among them, the effectiveness of our policing of that minority of physicians whose actions bring discredit and trouble to all of us. . . .A critic of the schools is no more automatically an enemy of education than a music credit is an enemy of music. By the same token, a sincere critic of bad medicine can be the best kind of friend for good medicine.

—Dr. Gunnar Gundersen, President of the A.M.A.

In recent years medicine may have suffered more from its successes than from its failures. Progress in postponing death has come so rapidly in the past several decades that we must now recognize that the rate of progress can scarcely be continued at its frenzied pace.

—Committee to Study A.M.A. Objectives and Basic Programs.

Not only are the ladies [of the Woman's Auxiliary] a charming, indispensable, stimulating part of our everyday lives, aiding most in preventing us from regarding our professional work as a chore, but they also play a very vital part in Medicine in our country.

—Report adopted by House of Delegates.

There are approximately 1,500 companies in the health insurance field, and the character of the industry is such that the whole industry tends to follow, with comparable plans, once a few enter into a new phase of underwriting. Since some of the major companies are already active in provision of (1) coverage for an individual or for group enrollment for individuals over 65 and their families, and (2) "Paid-up" coverage at retirement, a rapid growth in such types of contracts may be expected in the future.

—Adopted report of Council on Medical Service.

It seems reasonable to assume that underwriting organizations, as well as health and welfare fund administrators, individuals and physicians need to understand the relative values of physicians' services if health insurance and similar mechanisms are to succeed and fulfill their potential in financing, either in full or in part, the cost incident to medical care.

—Committee on Medical Practices.

Of the 15 bills of a medical nature enacted into law by the 85th Congress, only one was opposed by the A.M.A. . . . In its statements to Congress the Association was supporting the legislation or principle involved on 19 occasions and was in opposition on only six occasions. We believe that these facts should be publicized to the American public and to the medical profession in order to help eliminate the oft-heard charge that the Association is basically negative in its approach to legislative matters.

—Report adopted by House of Delegates.

Whatever progress is to be achieved in the future cannot be made by unilateral action—whether by the medical profession or "third parties" in matters which intimately concern both groups. Problems and issues which have disturbed relationships in the past must be resolved on the basis of a mutual acceptance of responsibility, an understanding of the professional relationships and patient care involved, and other social and economic factors.

—Council on Medical Service.

A.M.A.'s House of Delegates, like the Congress, carries on its business openly. Our proceedings are of interest to both the profession and the public. Under these circumstances the failure to disseminate information regarding an important policy matter only stimulates rumor and misrepresentation. In the long run it is to our advantage, as well as the public and the profession, to make available factual, judiciously selected, information on matters under consideration as well as on those on which definitive action already has been taken.

—Adopted report of Board of Trustees.

War on Staphylococcus—Via New Training Aids Program

Spurred by the appearance of antibiotic-resistant Staphylococcus pyogenes var. aureus, a multiagency committee is bolstering the national program aimed at control of this bacterium in hospitals.

Known as the Interagency Committee for Training Aids on Staphylococcal Disease, the group was created through the efforts of six major health organizations: American Academy of Pediatrics, American College of Surgeons, American Hospital Association, American Medical Association, American Nurses Association, and the Communicable Disease Center of the U. S. Department of Health, Education, and Welfare.

An exchange of information on audiovisual and other training materials will be the aim of the new group. Mr. Ralph P. Creer, Director of Medical Motion Pictures and Television for the A. M. A., is chairman. The committee plans an immediate review of all existing training aids and will coordinate production, distribution, and utilization of future audiovisual materials.

The committee also hopes to avoid duplication of training aids and to encourage presentations that will best orient both professional and subprofessional groups to the increasing challenge posed by the Staphylococcus problem.

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Prescription Against Quackery Written by A.M.A. Bureau

The letter came to the A. M. A. Bureau of Investigation from a physician faced with a dilemma as old as quackery itself:

I have a young child as my patient. She has carcinoma of inoperable type. Relatives are trying to persuade the father to send her to Dallas for the Hoxsey treatment. My arguments against this would carry more weight if you could supply me with material regarding this treatment. Please send whatever information you have available.

The Bureau, in its report to the House of Delegates last month, noted that in the past year it had answered 3,200 similar inquiries. Some are from physicians; many more are from students, government agencies, Better Business Bureaus, and just plain hopeful, but slightly suspicious, laymen.

The Bureau's half-million index cards, carefully catalogued, provide a running history of modern charlatanry, a monument to man's gullibility in medical matters. But man need not be ignorant of the facts on "new" nostrums, machines, or treatments purported to relieve all the ills of mankind. The accumulated knowledge of the Bureau is available to both physicians and the public for the cost of a 4-cent stamp.

What sort of questions do they have, these correspondents? They vary from queries on the therapeutic qualities of garlic pills to the efficacy of vibrating mattresses as reducing aids, from hair growers to bust developers. There are trends, however, usually tied closely to diseases that have been heavily publicized.

Foremost among these for the past several years has been cancer, although the tempo has been falling off. Cancer questions reached a peak of more than 1,000 in 1955, but since then an increasing campaign in public education, effective enforcement of the Food and Drug Act, the death of two cancer quacks, and the closing of a Missouri "institute" have slowed the stream.

Other popular subjects of late have been alleged "rejuvenators" (especially Royal Jelly), vitamin preparations, reducing aids, and the many gadgets of the ingenious quack.

The Bureau—headed by Mr. Oliver Field, an attorney with a background of investigative experience—cooperates closely with law enforcement agencies, offering information on request and adding data from these agencies to Bureau files where applicable. The federal Food and Drug Administration, the Post Office Department, and the Federal Trade Commission are no strangers to Field. Often the Bureau's files have been helpful to them as source material for their investigations.

In addition to answering mailed queries, Field makes an average of 50 talks a year before medical societies, civic clubs, PTA's, service organizations, and university groups. Field agrees only partially with Voltaire's opinion that "the charlatan was born when the first knave met the first fool." He believes that it is not the foolish but the ignorant or misinformed who are the ready victims of quackery.

Secrets Which Doctors Should Not Keep

More than one petty thief has hit the big time at a doctor's expense—and there is some evidence that the apathy of the victim may be giving such a criminal a push up the ladder of "success." The following selected recent newspaper accounts indicate a rising trend of stealing from physicians:

—Late last summer, the Associated Press reported the case of Joseph Richard Gerard, who took $9,500 in cash and $12,420 in checks and securities from a safe in the home of a physician "friend" in New Athens, Ill. Gerard spent three months traveling and gambling in an attempt to get money to repay the doctor. Conscience-stricken, he finally gave himself up in San Antonio. According to the news report, "Mystified local authorities said the doctor had not reported the theft to them."

—Other thieves thrived on their victim's hesitancy to discuss his affairs last year, when $245,000 in stocks were stolen from a Lancaster, Pa., retired physician. According to the *New York Times*, 82-year-old Dr. Donald M. Myers returned from town one night to find three men waiting for him. They escorted him inside his home, tied him up, and broke open his desk. There they found 22,313 shares of stock. Dr. Myers freed himself after the robbers left, but it was not until 10 days later that he told a friend—and swore him to secrecy.

"It might have remained a general secret," the *Times* reported. But two months later a man assumed the identity of the aged doctor and tried to sell the securities to a brokerage firm, which became suspicious and found out they had been stolen.

—According to the *A.M.A. News*, two "patients," working separately, made a healthy profit on the principle that doctors also have neither the time nor the inclination to check up on bank accounts.

The A.M.A. Bureau of Investigation is working with police by alerting the profession to operations of such bogus check passers and other swindlers. Oliver Field, director of the Bureau, says:

"Swindlers and thieves are free to steal again whenever their victims keep silent. Physicians, particularly, have a duty to protect fellow practitioners, as well as all fellow citizens, by reporting such crimes immediately to police."

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SMALLPOX TODAY

VIVID impressions have been recorded by Prof. A. Herrlich of a severe smallpox epidemic that began in East Pakistan and came to involve India. Herrlich was permitted by the Public Health Service in Bombay to spend four weeks at the City Fever Hospital, where he was able to examine more than 500 smallpox patients. He returned to Germany with much valuable material, including continuously refrigerated specimens of blood and tissues. The rapid progress of virology in recent years and the reports of new methods for cultivating the smallpox virus enhance the value of such material.[1] In addition, Herrlich has published photographs that strikingly illustrate the course of smallpox in its severe forms.[2] These should be of special interest to physicians in countries like the United States, where "classical" smallpox is absent and the diagnosis of cases made mild by vaccination has become difficult.[3]

The cases seen by Herrlich were of the worst kind. He saw more than one patient whose head seemed to be covered by a single confluent lesion, with mouth and nose so obstructed by swollen tissues and purulent discharges that the drinking of water became impossible, tracheotomy was out of the question, and asphyxia could only be postponed by giving oxygen through a nasal catheter. He saw patients lying practically immobilized in an armor of crusts that covered pus, blood, and indurated tissue. In one patient who recovered, the process of desquamation included the shedding of the soles of both feet.

At the height of the outbreak in Bombay there were 450 smallpox patients at this hospital, many of them sheltered in large emergency tents and cared for partly by relatives and friends. The picture is worth keeping in mind, for the adequacy of our medical, nursing, and hospital facilities in the face of possible epidemics of this magnitude needs to be reviewed from time to time. Herrlich pays tribute to the untiring efforts of the young Indian physicians and nurses, overwhelmed as they were by this encounter with a disease for which there is still no direct remedy. There was also a shortage of antibiotics. They do not prevent the multiplication of the smallpox virus but they are important in controlling secondary infections. The incidence of such infections—abscesses, secondary pneumonia, orchitis, osteomyelitis, and others—was alarmingly high. It might well have been reduced had it been possible to use antibiotics on a larger scale.

Smallpox is still endemic in some parts of the world and is still being carried about by international travelers. The World Health Organization has reported [4] that no less than 18 countries were thus infected with smallpox in the year 1956. The disease was successfully localized in 10 countries, but epidemics started in 8. In 1956 WHO stated [5] that "for the past 5 years 58% of all cases were reported from India and Pakistan." It was further stated that "The Indian sub-continent (India and Pakistan) is at present the principal endemic reservoir of variola major, with high mortality. Vaccination and previous attacks have not yet built up a sufficient proportion of protected population." [6] In 1958 WHO reported, further, that the incidence of smallpox in India was rising.[7] It appears that these were the signs presaging the "smallpox year" that Herrlich witnessed.

People who have never seen smallpox may find it hard to maintain that feeling of conviction that is needed to run a continuous program of vaccination. On this point Herrlich, who is director of the Bavarian State Vaccination Institute writes with emphasis: "The only way to combat smallpox is to vaccinate, and the only way to avoid the complications of vaccination would be not to vaccinate. But in all our discussions of the advantages and disadvantages of vaccination we should not belittle the importance of smallpox as a disease . . . It continues to defy the exertions of physicians and remains as treacherous as it was in the days of the Arabs who first described it."

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COUNCIL ON MEDICAL SERVICE

HOW OLD IS TOO OLD TO WORK?

Interesting clues, with specific application to retirement, as to the answer to the question, "How old is too old to work?" have been reported by S. L. Pressey, professor of psychology at Ohio State University, under the title of "Jobs at 80."[1] Although this study pertained more to persons now living, some surprising examples of performance during the latter decades of life were taken from eras when the average life expectancy was far below the approximately 70 years prevailing today. The studies of Lehman[2] are cited in the following examples: Gladstone was prime minister at 84; a number of our Supreme Court justices served well into their eighth decades (Holmes was 90 when he retired); Tennyson was 80 when he wrote "Crossing the Bar"; Belline at 83 painted one of his masterpieces; Robert Bridges and Thomas Hardy at 85 published poetry that has been long remembered; Verdi was composing at 85; Alexander Humboldt at 89 published his "Cosmology"; and Wundt completed his reminiscences at the age of 88.

Lehman lists 94 persons who continued to produce well into their later decades, 29 of whom produced works of importance at the ages of 80 or over. Pressey points out that, while Lehman's data clearly indicate that the best creative work in the arts and science is usually accomplished quite early in life, his research gives abundant evidence that the creative mind may continue to be productive well into the later years of the life span.

Of more current interest—how about those living and working today into their eighth decades, and further, those engaged in more ordinary areas of activities.[2] Pressey, instead of employing a systematic sampling procedure, merely made an effort to find out if there were such cases of octogenarians, and, if so, of what types. Three sources were explored for case material.[3] 1. Extensive case records of 230 superior older persons in a midwest city. Result: 35 were 80 years of age or over and, of these, 19 were at least occasionally doing some remunerative work. 2. Reports from a total of over 1,000 university students concerned with such problems; these students were requested to report their knowledge of well-known older persons who had done paid work. Result: A total of 127 persons were reported, all of whom were 80 years of age or over and, of these, 9 were 90 or over. 3. A collection of clippings regarding older persons; only those clippings were used which seemed essentially valid. Result: 167 persons past the age of 80 were reported as doing some work.

The three sources which were utilized produced 313 persons aged 80 or over (23 were 90) who were still earning money—who were gainfully employed. Most of the nonagenarians were working either part time or occasionally and included two clergymen, three physicians, three lawyers, one 94-year-old woman who was a receptionist, one man who was justice of the peace, another who operated a cigar stand part time, and one who trained dogs for driving livestock. However, a few were still employed full time; two were bank presidents in small towns; one was a bank teller; and a woman aged 90 was continuing her insurance business.

Among others, all over 80 years of age, but not necessarily 90, were three persons who wrote columns for their local papers, a wood carver who was retouching and restoring paintings and church frescoes, a chemist who was consultant for an industrial organization, a biologist who was consultant for a research institute, and another who published a history of his specialty.

Professional people constituted the largest group (18 physicians and 12 lawyers) but there were 24 skilled artisans, 8 farmers, 8 owners of small stores, 3 clerks, 2 barbers, and several handy men.

Pressey points out that, in view of the informal method of the survey, the figures mean nothing except to show that in all work categories some persons continue useful work into the eighth and ninth decades.

To the above figures probably should be added an undetermined number of persons who had the capacity to work but lacked either the desire or the necessity, and those who had these characteristics but for whom no work was available.

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MEDICAL NEWS

CALIFORNIA

Heart Symposium in Los Angeles.—Twenty local investigators will present papers on cardiovascular diseases at the third annual Midwinter Symposium of the Los Angeles County Heart Association at the Statler Hotel Jan. 14. The symposium is free to all physicians. Dr. John L. Denney is chairman of the all-day session, which will begin at 9 a. m. and will feature studies in basic sciences, clinical research, and heart surgery. The annual Oliver P. Douglas Memorial prize essay award and honorable mention award will be presented at a luncheon meeting by Dr. Edward Shapiro, past-president of the association.

COLORADO

Combined Meeting in Colorado Springs.—The American College of Physicians, Colorado Region, and the Colorado Society of Internal Medicine will hold a combined meeting at the Broadmoor Hotel, Colorado Springs, Jan. 16-17. Guest speakers include Dr. Philip S. Hench, Rochester, Minn., regent of the college and Dr. H. Marvin Pollard, Ann Arbor, Mich., governor of the college for Michigan. Dr. C. F. Kemper is governor of the college for Colorado, and Dr. William A. H. Rettberg is President of the Colorado Society of Internal Medicine. Three panel discussions are planned with the following moderators:

The Prevention and Management of Hepatitis, Dr. Fred Kern Jr., Denver.

Recent Developments in Rheumatic Diseases, Dr. Charley J. Smyth, Denver.

Anxiety in Clinical Medicine, Dr. Franklin G. Ebaugh, Denver.

For information write Mr. E. R. Loveland, 4200 Pine St., Philadelphia 4.

FLORIDA

Dr. Eyster Honored.—Dr. John A. E. Eyster, of Fort Meyers, emeritus professor of physiology who retired from the University of Wisconsin Medical School, Madison, in 1952, has been honored for "incisive, productive, and humane experimental science" by the Medical Research Association of California which awarded Dr. Eyster its Senior Scientist Award for 1958. In reviewing his research career, the association cited Dr. Eyster for "inspired graduate and medical teaching, and for devotion to the advancement of medicine through animal research."

Physicians are invited to send to this department items of news of general interest, for example, those relating to society activities, new hospitals, education, and public health. Programs should be received at least three weeks before the date of meeting.

ILLINOIS

Chicago

Dr. Hesseltine Named Ryerson Professor.—Dr. Henry C. Hesseltine, professor and secretary, department of obstetrics and gynecology, University of Chicago, has been named Mary Campau Ryerson Professor of Obstetrics and Gynecology. Mary Campau Ryerson was the mother of the late Martin A. Ryerson, member of the Board of Trustees of the University from 1890 to 1931 and president from 1892 to 1922 who died in 1932 and who established the Mary Campau Ryerson professorship Dec. 11, 1930, as a tribute to his mother. Dr. Hesseltine became an instructor in obstetrics and gynecology at the University of Chicago in 1931, assistant professor in 1934, associate professor in 1942, secretary of the department and professor in 1949. His appointment to the named chair became effective Nov. 11. He is president of the Chicago Gynecological Society and a diplomate of the American Board of Obstetrics and Gynecology.

LOUISIANA

Graduate Medical Assembly.—The 22nd annual meeting of The New Orleans Graduate Medical Assembly will be held March 2-5, with headquarters at the Roosevelt Hotel. Eighteen guest speakers will participate, and presentations are planned to be of interest to specialists and general practitioners. The program will include 54 discussions in addition to clinicopathologic conferences, symposiums, medical motion pictures, round-table luncheons, and technical exhibits. Following the meeting, arrangements have been made for a clinical tour to Mexico City, Cuernavaca, Taxco, Acapulco, and San Jose Purua, leaving New Orleans March 6 and returning March 21. Information is available at the office of the Assembly, Room 103, 1430 Tulane Ave., New Orleans 12.

MARYLAND

Dr. Lillie Receives Award.—The first Sustaining Membership award of the Association of Military Surgeons of the United States was given to Dr. Ralph D. Lillie, chief of laboratory and histochemistry, National Institute of Arthritis and Metabolic Diseases, National Institutes of Health, Bethesda, "for his accomplishments in the field of histochem-

istry" at the recent meeting of the association. This award, consisting of a scroll and an honorarium of $500, is given by the Sustaining Membership Group of the association to government employees who have distinguished themselves by "outstanding work in the field of research."

MASSACHUSETTS

Lectures on Medicine and Law.—The Right Honorable Lord Nathan, P. C., of England, spoke on "Medical Negligence and the Law" at Boston University School of Medicine, Nov. 18. Lord Nathan was the first speaker in a series of lectures sponsored by the Boston University Law-Medicine Research Institute. Director of the Institute is Prof. William J. Curran of Waban, Mass. Lord Nathan is a member of the International Law Association, Medico-Legal Society, and the British Section, International Commission of Jurists (Member of Council). Future speakers in the series sponsored by the institute will talk on Law and Behavioral Science; Heart Disease and Stress; Demonstrative Medical Evidence; Medicine, Morals and The Law; and Accidents and Accident Repeaters.

MICHIGAN

Establish Gordon B. Myers Award.—The Gordon B. Myers award in internal medicine has been established at Wayne State University College of Medicine, Detroit, "in recognition of Dr. Myers' inspiring leadership as chairman of the department of medicine for over 20 years." The award has been made possible by contributions from former residents and fellows who received postgraduate training under Dr. Myers. An award of $100 and a scroll is to be made annually to the graduating senior who has distinguished himself above all others in his class in courses given by the department of medicine. The recipient of the award will be chosen by the chairman and the full-time faculty of the department. Dr. Myers resigned as chairman of the department of medicine in 1958. As professor of medicine, he heads the university service in internal medicine at Harper Hospital.

MINNESOTA

Guest Lecture.—Mr. R. Milnes Walker, professor of surgery in the University of Bristol, Bristol, England, gave a lecture on "Some Problems of Portal Hypertension" at the Mayo Clinic and Mayo Foundation, Rochester, Nov. 7.

NEW JERSEY

Typhoid Fever.—The National Office of Vital Statistics has revealed that Dr. Hugh D. Palmer, New Jersey district state health officer, reported an outbreak of six cases of typhoid fever in a community of about 1,000 population. On Oct. 24 a 42-year-old woman died with a tentative diagnosis of typhoid fever. This diagnosis was subsequently confirmed. By Nov. 8 other cases had developed in five persons ranging in age from 2 to 16 years. The diagnoses were confirmed by isolation of *Salmonella typhi* from stool specimens and/or agglutination titers. Blood specimens were positive for "O" and "H" antigens. The community is without public water and sewerage facilities. The houses in which the illnesses occurred have cesspools and shallow wells.

NEW YORK

Dr. Hodge Named Department Chairman.—Appointed as professor of pharmacology and chairman of the new department of pharmacology, University of Rochester School of Medicine and Dentistry, is Harold C. Hodge, Ph.D., who has been a professor of pharmacology and toxicology at the Atomic Energy Project of the medical center since 1946.

Society News.—The Medical Society of the State of New York, 750 Third Ave., New York 17, has announced the appointment of Dr. Herbert T. Wagner as executive director.—The officers of the New York Allergy Society for 1958-1959 are as follows: president, Dr. Aaron D. Spielman, New York City; president-elect, Dr. S. Senior Sack, Flushing; vice-president, Dr. Russell C. Grove, New York City; secretary, Dr. Sheppard Siegal, New York City; treasurer, Dr. Joseph H. Fries, Brooklyn; and assistant secretary-treasurer, Dr. Murray Dworetzky, New York City.

New York City

Memorial Fellowship in Dermatology.—Phi Delta Epsilon Fraternity's Charles R. Rein Memorial Fund has awarded a fellowship in dermatology to New York University. It honors the late Dr. Charles R. Rein of the department of dermatology and syphilology of the NYU Post-Graduate Medical School and is to go annually to the candidate selected by Dean Donal Sheehan and the chairman of the department of dermatology and syphilology. Dr. Laszlo Biro, a resident in the dermatologic service at The Bellevue Hospital Center, has been selected to be the first recipient of the fellowship. He will engage in research on the serology, immunology, and epidemiology of treponemal and staphylococcal diseases and other infections. The three-year fellowship, made possible through the contributions of fraternity members and friends to a memorial fund, was established in May, 1957, on the death of Dr. Rein, a past-grand consul of the fraternity.

Personal.—Dr. H. Houston Merritt, acting dean of the Faculty of Medicine and acting vice-president in charge of medical affairs at Columbia Univer-

sity College of Physicians and Surgeons, has been elected a vice-president of United Cerebral Palsy Associations Inc., at the organization's ninth annual conference.——Dr. Abraham M. Rabiner has been named professor emeritus of neurology at the State University of New York Downstate Medical Center in Brooklyn. A member of the center's faculty since 1937 when it was still the Long Island College of Medicine, Dr. Rabiner retired as professor and head of the division of neurology on Aug. 31. On the same date he retired as director of neurology at the Kings County Hospital.——Dr. Frederick S. Reiss, associate clinical professor of dermatology, New York University, Postgraduate Medical School, has been elected honorary member of the Sociedade Portuguesa de Dermatologia e Venereologia.

NORTH CAROLINA

Program to Aid Child Amputees.—The Duke University Medical Center's Orthopedic-Amputee Clinic has been selected to participate in a national program aimed at helping child amputees. Sponsored by the Prosthetic Research Board of New York University under the National Research Council, the program will help parallel for children the progress made in artificial limbs for veterans since World War II. Also, the program will promote the expansion of child amputee clinics throughout the United States. The Duke amputee clinic, headed by Dr. J. Leonard Goldner, professor of orthopedic surgery, is one of nine chosen to take part in the program. Beginning Jan. 1, the Duke clinic will collect special data on the problems and progress of all amputee patients under 16 years of age. This and similar information gathered at other amputee clinics over the nation will be brought together during periodic meetings of clinic heads. Other amputee clinics participating with Duke in the new program are located in Atlanta, Ga.; Birmingham, Ala.; Philadelphia; Grand Rapids, Mich.; Buffalo, N. Y.; Los Angeles; Chicago; and New York City. The Duke clinic, established in 1955, uses a team approach to the problems of amputees. Team members include an orthopedic surgeon, a prosthetist (artificial limb maker), a physical therapist, an occupational therapist, and a social service worker.

OHIO

Dr. Beck Gives Kuntz Lecture.—Dr. Claude S. Beck, professor of cardiovascular surgery, Western Reserve University School of Medicine, Cleveland, delivered the annual Albert Kuntz lecture Dec. 15 on "Coronary Heart Disease Blood Supply to Ischemic Muscle." The lecture is sponsored by the Phi Chi Medical Fraternity of the Saint Louis University School of Medicine.

Physicians Meeting in Cincinnati.—The Ohio Regional meeting of the American College of Physicians will be held at the Netherland Hilton Hotel, Cincinnati, Jan. 22, with Dr. A. Carlton Ernstene, governor of the college for Ohio, opening the program. Dr. Dwight L. Wilbur, president of the college, will be the principal speaker at the banquet at 7 p. m. A two-part clinical pathological conference will be conducted in the afternoon. A panel discussion on "Status of the Internist in Medical Care Plans" will be moderated by Dr. George J. Hamwi, Columbus. Sixteen papers will be read by title. For information write Dr. Eugene H. Sterne Jr., Veterans Administration Hospital, 3200 Vine St., Cincinnati 20.

OREGON

Plan Student Activities Building.—A new $350,000 Student Activities Building for the University of Oregon Medical-Dental School campus in Portland is being planned. At the late October meeting of the Oregon State Board of Higher Education, preliminary plans were approved and permission was given to finalize the blueprints for the two-story building. To be located in the canyon west of the Medical School Hospital and south of the Medical Science and Administration buildings, the 100- by 116-foot structure will be constructed of reinforced concrete and will include athletic and recreational facilities. A regulation size basketball court with seating areas will take up most of the second floor. Coordinating the planning of the facility has been W. A. Zimmerman, Medical and Dental School business manager. The building will be financed through student building fees which have been accumulating since 1945. About half the money needed is now available, and the rest will be made up through bonding of future building fee income.

PENNSYLVANIA

Meeting of Physicians in Philadelphia.—The American College of Physicians will hold its 20th annual reunion of Eastern Pennsylvanians at the Sheraton Hotel, Philadelphia, Jan. 23. The program is designed to encourage participation of physicians from all parts of Eastern Pennsylvania, and a cordial invitation is extended to physicians from Delaware and New Jersey. Dr. William A. Jeffers is governor of the college for Eastern Pennsylvania. Nineteen papers are scheduled for presentation at the three sessions. At the banquet at 7 p. m. with Dr. Allen W. Cowley Sr., Harrisburg, as toastmaster, Dr. Dwight L. Wilbur, San Francisco, president of the college, will give the address of the evening on "The Third Person in Medicine." For information write Mr. E. R. Loveland, Executive Secretary, American College of Physicians, 4200 Pine St., Philadelphia 4.

Philadelphia

Dr. Gyorgy Honored.—The University of Heidelberg has conferred the degree of honorary medical doctor on an alumnus and former faculty member, Dr. Paul Gyorgy, professor of pediatrics at the University of Pennsylvania, and chief of the pediatric service of the Philadelphia General Hospital. The honor, to Dr. Gyorgy, which was proposed by the faculty of Heidelberg, and approved by the Rector and the University Senate, was presented "in recognition of his many scientific achievements in the past." Also voted an honorary M.D. was Dr. Otto Warburg, of Berlin, a Nobel Laureate and developer of the Warburg Apparatus. Dr. Gyorgy is credited with the discovery of riboflavin.

Personal.—Dr. Henry L. Bockus, chairman, department of internal medicine, University of Pennsylvania Graduate School of Medicine, has been elected to membership on the executive committee of MEDICO, (Medical International Cooperation), a private, nonprofit organization that furnishes American medical personnel, techniques, drugs, and supplies to the newly developing countries of Asia, Africa, and Latin America. A division of the International Rescue Committee, MEDICO sends teams of American physicians and surgeons, and other types of private American medical assistance to areas of the world where they are needed.—Dr. I. S. Ravdin, John Rhea Barton Professor of Surgery, University of Pennsylvania, has been elected to the chairmanship of the Pennsylvania Plan to Develop Scientists in Medical Research at the recent meeting of the plan's executive committee, succeeding Dr. Norman H. Topping, formerly vice-president of the university who was appointed president of the University of Southern California, Los Angeles, in August.

TENNESSEE

Society Election.—The Memphis Thoracic Society, an organization of Memphis and Mid-South thoracic surgeons, internists, and medical chest physicians, has elected the following officers for 1959: Dr. Francis H. Cole, president, succeeding Dr. Felix A. Hughes Jr.; Dr. John C. King, vice-president; and Dr. Glenn E. Horton, secretary-treasurer (reelected). Physicians in the Mid-South area are invited to attend the meetings. Information may be obtained from the Secretary-Treasurer, Memphis Thoracic Society, 4915 Mockingbird Lane, Memphis 17, Tenn.

Walker Surgical Club Formed.—During the recent meeting of the American College of Surgeons in Chicago a club was formed in honor of Dr. Matthew Walker, chairman, department of surgery, Meharry Medical College, Nashville. The organization, to be known as the "Walker Surgical Club," is composed of surgeons who have received surgery training under Dr. Walker; there are presently 50 members in the club. At the organizational meeting Dr. Walker was presented with a silver tray bearing the inscription, "presented to Dr. Matthew Walker on the occasion of the founding of the Walker Surgical Club in deep appreciation of his unselfish service in the training of surgeons." Dr. Waldo L. Cain, Detroit, was elected chairman of the club and Dr. George W. Hilliard, secretary-treasurer. The club will meet once yearly during the meeting of the American College of Surgeons and has as its purpose the furtherance of the surgical program at Meharry.

TEXAS

Dr. Waksman to Lecture.—The Alpha Nu Chapter of the Phi Delta Epsilon Fraternity at the University of Texas Medical Branch, Galveston, will hold the Meyer Bodansky Lectureship Jan. 23. The guest speaker will be Selman A. Waksman, Ph.D., director, Rutgers Institute of Microbiology, New Brunswick, N. J.

Texas Society on Aging Formed.—Mr. Herbert Shore, of Dallas, has been chosen as first president of the new Texas Society on Aging, formed recently at the Driskill Hotel in Austin. Dr. Ernest W. Keil, Temple, is president-elect; Hiram J. Friedsam, Ph.D., Denton, is vice-president, and Mrs. William B. Ruggles, of Dallas, will serve as secretary-treasurer. The Texas Society on Aging is the product of a merger between the Texas Geriatric Society and the Texas Gerontological Society and carries as its slogan, "Aging is everybody's business." The new society has a membership of 600 and much of its work is in relation to the Texas Interim Legislative Committee on Aging. The Texas Society on Aging is a chapter of the national Gerontological Society, Inc., and is a nonpolitical, nonprofit, scientific society dedicated to fostering the growth and dissemination of knowledge relating to that process in medicine, physical and mental health and care, economics, employment, recreation, education, social welfare, housing and other fields, in order to advance the well-being of older persons in American culture. The society publishes a newsletter on developments in aging throughout the state and nation.

WASHINGTON

Plan Dedication of Teaching Hospital.—Dedication services for the new University of Washington Teaching Hospital have been set for April 18. Designed for teaching and research, the new hospital will accept referred patients from all parts of the state and will be a training center for 18 health

professions. Governor Albert D. Rossellini will be the principal dedication speaker. The hospital, adjacent to the Health Sciences Building at the southern edge of the university campus, has been built in two stages. Unit I, housing offices and laboratories

The new University of Washington Teaching Hospital, Seattle.

for departments concerned with patient care, was completed in 1954. Unit II, under construction, contains central service and diagnostic facilities, and outpatient clinic, and beds for 300 inpatients. The dedication will be followed by a public open house April 18 and 19.

GENERAL

Examinations by Board of Nutrition.—The American Board of Nutrition will hold the next examinations for certification as a specialist in human nutrition, during the week of April 12-18, 1959, in Atlantic City, N. J. Candidates who wish to be considered for these examinations should forward applications to the Secretary's Office not later than March 1. Application forms may be obtained from the Secretary, Dr. Robert E. Shank, Department of Preventive Medicine, Washington University School of Medicine, Euclid and Kingshighway, St. Louis.

Organize Institute of Medical Climatology.—On Nov. 20 the American Institute of Medical Climatology, a nonprofit organization, was officially formed in Philadelphia. Members include physicians, scientists, and educators. The institute sponsors a program of continuous research and education into all phases of the relationship between weather and human life. Twelve sections implement the work of the institute: medicine, biology, psychology, air pollution, biostatistics, institutional planning, industrial planning, atmospheric electricity, meteorology, public health, medical hydrology, engineering, and instrumentation. Charter members of the institute have elected the following officers: Dr. George M. Piersol, president; Very Rev. James A. Donnellon, O.S.A., first vice-president; and Harold W. Schaefer, second vice-president. Dr. Igho H. Kornblueh, 1618 Allengrove St., Philadelphia 24, is secretary.

Bahamas Serendipity Conference.—The first Bahamas Serendipity Conference will be held Jan. 18-31 at the British Colonial Hotel, Nassau, Bahamas. The conference "aims at bringing together people from various disciplines, research workers, scientists, and clinicians, to look together at a problem from their respective points of view." The following will participate as "animateurs" to stimulate discussion under the following themes:

Serendipity, R. Keith Cannan, D. Sc., Washington, D. C.
Kidney, Alfred Gilman, Ph.D., New York, N.Y.
Chemical Synthesis, Henry B. Hass, LL.D., New York City.
Discovery, Edward C. Kendall, Ph.D., Princeton, N.J.
Enzymology, Dr. I. Arthur Mirsky, Pittsburgh, Pa.
Scientific Accidents, Bernard Edward Schaar, Chicago, Ill.
Endocrinology, Dr. Abraham G. White, New York, N.Y.

Dr. B. L. Frank is the organizing physician for the Bahamas Conferences. Reservations should be made by writing directly to "Bahamas Conferences," P. O. Box 4037, Fort Lauderdale, Fla.

Report Lower Accident Rate for Large Cities.—A study by the Metropolitan Life Insurance Company's statisticians of accident mortality in the 41 U. S. cities which had 250,000 or more inhabitants at the time of the 1950 census has revealed that accident death rates for residents of these cities averaged 49.2 per 100,000 in 1955-56 as compared with 56.8 for the population of the U. S. as a whole. Of the 41 cities under review, 32 had rates below the national average. In spite of this, it is pointed out, residents of the large cities suffer a heavy loss of life from accidents, each year about 18,000 of them being fatally injured in mishaps of one kind or other. The accident death rate in 1955-56 in the large cities ranged from a low of 37.8 per 100,000 for Jersey City to a high of 77.7 for Indianapolis. The five cities with one million or more inhabitants in 1950—New York, Chicago, Los Angeles, Philadelphia, and Detroit—as a group experienced a lower rate than did groups composed of the cities with populations in various ranges under one million. For the 41 cities as a group, the motor vehicle accident death rate was about 31% below the national average.

Listing of Government Scientific Information.—The National Science Foundation has published the first bulletin in a new series which, when completed, will represent an inventory listing of all significant scientific information sources or activities within the federal government. Reportedly, the series should prove of value as an aid in directing scientists, engineers, and research librarians to the appropriate sources of government-sponsored or -supported research information in specific scientific fields. The preparation and publication of this series is one of the tasks undertaken by the foundation's Science Information Service

under its Unpublished Research Information (URI) program. The primary objective of this program is to make unclassified unpublished scientific research information easily accessible and readily available to all U. S. scientists and engineers, in and out of government. Comments or suggestions concerning the intended purpose of this series, as well as the contents of specific issues, should be addressed to: National Science Foundation, Science Information Service, Washington 25, D. C., Attention: URI Program Director.

Awards in Anesthesiology.—The first Mead Johnson awards for graduate training in anesthesiology have been granted to three physicians. Dr. Ralph S. Sappenfield, of Miami, Fla., president of the American Society of Anesthesiologists, has announced that the society would award the scholarships annually. The scholarships are made possible by funds granted by Mead Johnson & Company, Evansville, Ind. Recipients of the first awards are: (1) Dr. Robert Douglas Winship, Berkeley, Calif., a resident physician at the University of California Hospitals, San Francisco; (2) Dr. Jack Allan Gray, Dallas, Texas, who has been a resident physician in anesthesiology at Parkland Memorial Hospital since July, 1957; and (3) Dr. Thomas Franklin Wooden, who will become a resident physician in anesthesiology at Indiana University Medical Center, Indianapolis, following completion of Army service. The Mead Johnson awards are made to physicians engaged in residency training for specialization in anesthesiology, and are granted to "deserving physicians on the basis of meritorious work in clinical and research fields, and general qualifications for success in the specialty." Selection of physicians is carried out in behalf of the society by trustees of the Anesthesia Memorial Foundation, headed by Dr. John S. Lundy, of Rochester, Minn.

Society News.—New officers of the **Southwestern Dermatological Society** elected at Tucson are: Dr. Earle R. Pace, Santa Fe, president; Dr. George A. Waldriff, Albuquerque, vice-president; Dr. Henry D. Garrett, El Paso, secretary-treasurer.—Dr. Leona Baumgartner, New York City, became president of the **American Public Health Association** at the conclusion of its 86th annual meeting in St. Louis Oct. 27-31. Dr. Malcolm H. Merrill, Berkeley, was named president-elect, and will become president at the 87th annual meeting in Atlantic City Oct. 19-23, 1959. Vice-presidents elected were Drs. Abraham Horwitz, Santiago, Chile; Frederick B. Roth, Regina, Saskatchewan, Canada; and Estella Ford Warner, Albuquerque, N. M. Executive director is Dr. Berwyn F. Mattison, with headquarters at 1790 Broadway, New York 19.—New officers of the **American Society of Anesthesiologists** are as follows: president, Dr. Daniel C. Moore, Seattle, succeeding Dr. Ralph S. Sappenfield, Miami, Fla.; president-elect, Dr. Leo V. Hand, Boston; first vice-president, Dr. William O. McQuiston, Peoria, Ill.; second vice-president, Dr. George J. Thomas, Pittsburgh; secretary, Dr. Joseph E. Remlinger Jr., Chicago; assistant secretary, Dr. Robert L. Patterson, Pittsburgh; treasurer, Dr. Albert M. Betcher, New York City; assistant treasurer, Dr. Edwin Emma, Flushing, N. Y.

Awards to Medical Students.—The five winners in each of three divisions of the 1958, 13th annual Schering Award Competition have been announced by Dr. Richard McCormick, chairman of the award committee. Fifteen winners shared in the $5,700 prize money established by Schering Corporation, with individual prizes ranging from $1,000 for first prize, to $50 for fifth prize. Marvin Gottlieb, of the University of Tennessee College of Medicine, Memphis, who has won two similar awards in 1956 and 1957, received $1,000 for his paper on "The Mechanism and Current Concepts on the Treatment of Nausea and Vomiting." Frank A. Oski, of the University of Pennsylvania School of Medicine, Philadelphia, also received a first prize of $1,000 for his paper, "Current Trends in Corticosteroid Therapy in Pediatrics." The third first-place winner was Mrs. Helen S. Kaplan, of the New York Medical College, New York City, who received $1,000 for her paper on "Use of Tranquilizer Therapy in Office Practice." The three second-place winners receiving $500 each for their prize winning papers are: Marvin Anderson Jr., University of Michigan Medical School, Ann Arbor; Martha Bouck, of Queen's University Faculty of Medicine, Kingston; and Larry Samuels, University of Illinois College of Medicine, Chicago. Third, fourth, and fifth place prizes were of $250, $100, and $50, respectively. The Schering award, which began in 1940, seeks to encourage among the nation's medical students original reporting and exploration of recent developments in therapy.

Scientific Exhibit Assembly.—Medical students, interns, and residents are being urged to participate in the second annual national scientific exhibit assembly of the Student American Medical Association to be held in Chicago April 30-May 2. The program was inaugurated in 1958 and is dedicated to the contributions of medical students to research and to the advancement of the scientific exhibit as a primary medium of communication in the profession. Arrangements have been made for space to hold a total of 40 scientific exhibits; of these, 20 will be by students and 20 by interns and residents. The SAMA-Lakeside Laboratories awards will again be given, with the special honor of free all-expense trips to the American Medical Association convention and the privilege of exhibiting in

the AMA's scientific assembly, for the top student and the top intern or resident. Cash prizes and plaques will be given, with $500, $250, and $100 for award-winning exhibits by students, and equal awards for those by interns and residents. Lakeside Laboratories supports the awards and the trips. Applications must be obtained from SAMA (address Mr. Russell Staudacher, Executive Secretary, Student American Medical Association, 430 N. Michigan Ave., Chicago 11) and returned no later than Feb. 1, 1959. On Feb. 14, the 40 chosen exhibitors will be announced. These must complete their exhibits and ship them to Chicago at their own expense. Space and basic materials such as backdrop, table, chairs and lighting, will be provided free by SAMA.

Program for Health Scholarships.—The National Foundation, to help overcome shortages of personnel in the health field, has announced a multimillion-dollar scholarship program, a first step in its new expanded program. The present scholarship and fellowship program will be continued but modified and expanded where necessary. This program over the years has added over 7,600 especially trained people to those prepared to work in research and patient care. Mr. Basil O'Connor, president of the foundation, summarized the new program as follows:

The National Foundation will offer annual health scholarships to help provide four years of College education in medicine, medical social work, nursing, physical therapy, and occupational thearpy.

A minimum of 505 Health Scholarships will be offered each year, the first of them before the end of the 1959 school year. They will be made available on a geographic basis with heavily populated states receiving as many as 25—or five for each of the five professions—and with no state or territory receiving less than five health scholarships, a minimum of one for each of the five professions.

The foundation's chapters, numbering more than 3,100 will seek and accept scholarship applications, pass them on to state or territorial professional committees for selection, and will present awards to winners.

Health scholarships will be available to student citizens of the U. S. in the 49 states, the District of Columbia, Hawaii, and Puerto Rico.

Over the next 10 years this program will cost at least $12,000,000. Each scholarship awardee will receive $500 a year for four years, or a total of $2,000, providing that scholastic standards are maintained. The 505 health scholarships each year will cost over one million dollars.

Because education requirements of the five professions vary, scholarships will be made available in nursing, physical therapy and occupational therapy to graduating high school students; in medical social work, at the college junior year, extending through two years of required graduate work; and in medicine, at the college junior, senior, or first graduate year, depending upon the requirements of the medical school. For information write the National Foundation, 800 Second Ave., New York 17, N. Y.

Tuberculosis Among Kindergarten Children.—A community-wide study of the tuberculin test among kindergarten children, conducted in Kansas City, Mo., with the aid of a Christmas Seal grant from the National Tuberculosis Association and its medical section, the American Trudeau Society, has revealed a relationship between the size of the test and the presence of active tuberculosis among adults in contact with the children; it also revealed that there was no decrease in tuberculosis infection rates among kindergarten children in the 10-year period of the study, despite a marked decline in tuberculosis mortality in the community. In the survey the histoplasmin test for histoplasmosis infection was given as well as the skin test for tuberculous infection. During the period covered, from 1947 to 1957, the tests were given 35,995 kindergarten children. For seven years, nonreactors to tuberculin were retested in the first grade and it was found that, on the average, 1% of the white children and 1.4% of the Negroes had converted to positive. The rate of conversion did not fall during the period covered. The study showed that a number of new previously unknown cases of tuberculosis was found in a follow-up of the adult contacts. The percentage of children who became infected during the first year in school was relatively high and showed no tendency to decline over the period of seven years' observation. This was despite the fact that the death rate from tuberculosis for Kansas City fell during the 10 years of the survey from 31.3 to 11.7. On original testing in kindergarten, there were 597 reactors to tuberculin among the 35,995 children, the percentage being higher among the Negro children than among the white children; conversely, the percentage of reactors to histoplasmin in this city where histoplasmosis is endemic was higher among the white children. The Heart of America Tuberculosis Association, Kansas City, Mo.; the University of Kansas School of Medicine, Kansas City, Kan.; the Kansas City, Mo., Board of Education; and the Communicable Disease Center, U. S. Department of Health, Education, and Welfare, Atlanta, Ga., cooperated in the study.

Levels of Radioactivity in Milk.—The U. S. Public Health Service has reported that radioactivity levels in milk collected during August from 10 sampling stations across the country continued to be below the current permissible levels recommended by the National Committee on Radiation Protection and Measurements. Radiation levels from six stations showed a decline in strontium-90 compared with July data. These were the stations in the milksheds serving Austin, Texas; Cincinnati; Fargo, N. D.; New York City; Salt Lake City; and St. Louis. Three stations, in the milksheds serving Atlanta, Ga., Chicago, and Sacramento, Calif., reported slight increases over July. A tenth station,

in the milkshed serving Spokane, Wash., was added to the network in August. Levels of four other specific radioactive elements in milk—iodine-131, strontium-89, barium-140, and cesium-137—were also found to vary not only between samples collected from different stations of the network, but, also, between samples taken from the same stations. From past experience, month-to-month fluctuations in levels reportedly are to be expected. The National Committee on Radiation Protection and Measurements is a scientific group established under the sponsorship of the National Bureau of Standards with the cooperation of radiological organizations in the United States. The permissible levels recommended by the committee refer to average exposure over an entire lifetime and may be exceeded for short periods of time. The levels are subject to periodic evaluation and revision as new scientific data become available. Monthly composite samples of milk obtained through the cooperation of state and municipal health agencies, state departments of agriculture, and the dairy industry are analyzed for specific radioactive elements at the Robert A. Taft Sanitary Engineering Center operated by the Public Health Service in Cincinnati. About six weeks are required to complete the laboratory analysis of the samples. Average exposure over an extended period of time reportedly is the significant factor in interpreting the public health effects. Data are reported in terms of micromicrocuries per liter. For the period ending August, 1958, the 12-month average levels for these elements were: strontium-90 ranged from 4.2 to 10.7; iodine-131, from 29 to 220; strontium-89, from 24 to 115; barium-140, from 17 to 95; cesium-137, from 53 to 73.

FOREIGN

Award in Laryngology.—The International Committee for the Gould Award has announced that the selection of the recipient for the year 1958 is Prof. Fumio Nakamura, M.D., Kyoto Prefectural Medical College, Kyoto, Japan, for his electrophysiologic studies of laryngeal function. The Gould award is presented annually for "outstanding research in laryngology" to encourage and reward fundamental investigations in this field. The international committee for 1959 will consist of Sir Victor Negus, 149 Harley St., London, W.1; Prof. Cotoji Satta, No. 111 Morikawa-cho, Bunkyo-ku, Tokyo; and Dr. Hans von Leden, Medical Director, The William and Harriet Gould Foundation, 30 N. Michigan Ave., Chicago 2. The amount of the award has been increased to $300.

Medical School and Teaching Hospital in Belgian Congo.—Founded three years ago under the sponsorship of the University of Louvain, one of the oldest schools in Europe, Lovanium University in Leopoldville, the Belgian Congo, is making progress toward the organization of a complete university curriculum. To assist in the development of the medical school and the university hospital, The Rockefeller Foundation has appropriated 10,952,500 Belgian Congo francs (about $230,000) for use during the next three years. When the medical school opened in 1954, five students were enrolled; this number has now risen to 37, of whom 15 are in the first year of the course. The formative years of the school have been devoted primarily to the basic sciences and morphological studies. By the time the students reach the clinical stage of their training, the new university hospital is expected to be ready for use. The university obtained the hospital at 20% of its actual cost through an agreement to operate it for the medical needs of the region for which the government is responsible. When completed, the hospital will have a capacity of 1,000 beds and represent an investment of 4 million dollars. Two wings are in operation. The university has undertaken responsibility for public health activities in two nearby native villages, Ndjili and Matete, with a combined population of 14,000. University students, who will participate in the medical and health services, will have direct practical experience with community problems as well as with in-patients in the university hospital. The new university is coeducational and permits no racial, religious, or political discrimination. At present the university consists of a Faculty of Science which is preparing students for studies in medicine and agriculture; the Faculty of Medicine; a Faculty of Administration and Social Science which is to become a College of Law; and a Faculty of Education which is now preparing teachers for the secondary schools of the Congo and which will later be developed into a College of Liberal Arts. The Government of the Congo, the Mining Union, and private sources are all contributing to the construction of university buildings.

CORRECTIONS

Treatment of Metastatic Thyroid Carcinoma.—In the Question and Answer concerning metastatic thyroid carcinoma (THE JOURNAL, Dec. 6, 1958, page 1953) in the 10th line of the answer the symbol "μc" for microcurie was given instead of mc. for millicurie.

Journal "Backbones" December 27.—Some 20,000 copies of THE JOURNAL of Dec. 27, 1958, had been mailed before it was discovered that the wrong date (Dec. 17) had been printed on the "backbone" of those copies. The date on the front cover and inside the Dec. 27 issue is correct. We regret that this error occurred.

EXAMINATIONS AND LICENSURE

NATIONAL BOARD OF MEDICAL EXAMINERS

National Board of Medical Examiners: Part II only, April 21-22; Parts I and II, June 16-17; Part I only, Sept. 9-10. Examinations must be received at least six weeks in advance of a specific examination date. Examining centers established after close of registration. Exec. Sec., Dr. John P. Hubbard, 133 South 36th St., Philadelphia 4.

EDUCATIONAL COUNCIL FOR FOREIGN MEDICAL GRADUATES, INC.

Educational Council for Foreign Medical Graduates, Inc.: Stations around the world, Feb. 17. Deadline for foreign applications was Nov. 17. The following examination will be held Sept. 22 with application deadline of June 22. Exec. Director, Dr. Dean F. Smiley, 1710 Orrington Ave., Evanston, Ill.

BOARDS OF MEDICAL EXAMINERS

ALABAMA: *Written.* Montgomery, June 16-18. Sec., Dr. D. G. Gill, State Office Bldg., Montgomery 4.

ALASKA:* On application in Anchorage and Juneau. Sec., Dr. W. M. Whitehead, 172 South Franklin St., Juneau.

ARIZONA:* *Written Examination and Reciprocity.* Phoenix, Jan. 14-16. Sec., Dr. Thomas H. Bate, 2910 North 7th Ave., Phoenix.

ARKANSAS:* *Examination and Reciprocity.* Little Rock, June 11-12. Sec., Dr. Joe Verser, Harrisburg.

CONNECTICUT:* *Regular. Examination.* Hartford, March 10-12. Acting Sec., Dr. Louis P. Hastings, 160 St. Ronan St., New Haven. *Homeopathic. Examination.* Derby, Jan. 13. Sec., Dr. Donald A. Davis, 38 Elizabeth St., Derby.

DELAWARE: *Written Examination and Endorsement.* Dover, Jan. 13-15, Jan. 22. Sec., Dr. Joseph S. McDaniel, Professional Bldg., Dover.

FLORIDA:* *Examination.* Miami Beach, June 22-24. Sec., Dr. Homer L. Pearson, 901 N.W. 17th St., Miami 36.

GEORGIA: *Examination and Reciprocity.* Atlanta, June. Sec., Mr. C. L. Clifton, 224 State Capitol, Atlanta 3.

GUAM: *Subject to Call.* Act. Sec., Dr. F. L. Conklin, Agana.

HAWAII: *Examination.* Honolulu, Jan. 12-13. Sec., Dr. I. L. Tilden, 1020 Kapiolani St., Honolulu.

IDAHO: *Examination and Endorsement.* Boise, Jan. 12-14. Sec., Mr. Armand L. Bird, 364 Sonna Bldg., Boise.

ILLINOIS: *Examination and Reciprocity.* Chicago, Jan. 26-30. Supt. of Registration, Mr. Fredric B. Selcke, Capitol Bldg., Springfield.

KANSAS:* *Examination.* Kansas City, Jan. 16-17. *Reciprocity.* Kansas City, Jan. 14. Sec., Dr. F. J. Nash, 364 New Brotherhood Bldg., Kansas City.

MAINE: *Examination.* Portland, March 10-12. *Endorsement.* Portland, March 10. Sec., Dr. Adam P. Leighton, 142 High St., Portland.

MASSACHUSETTS: *Examination.* Boston, Jan. 13-16. Sec., Dr. Robert C. Cochrane, State House, Room 37, Boston 33.

MICHIGAN:* *Examination.* Ann Arbor and Detroit, June 8-10. Sec., Dr. E. C. Swanson, 118 Stevens T. Mason Bldg., West Michigan Ave., Lansing 8.

MINNESOTA:* *Examination.* Minneapolis, Jan. 20-22. *Reciprocity.* St. Paul, February. Sec., Dr. F. H. Magney, 230 Lowry Medical Arts Bldg., St. Paul.

MONTANA: *Examination and Reciprocity.* Helena, April 7. Sec., Dr. Thomas L. Hawkins, 555 Fuller Ave., Helena.

NEBRASKA:* *Examination.* Omaha, June. Director, Mr. Husted K. Watson, Room 1009, State Capitol Bldg., Lincoln 9.

NEW HAMPSHIRE: *Examination and Endorsement.* Concord, Mar. 11-14. Sec., Dr. Edw. W. Colby, 61 So. State St., Concord.

NEW JERSEY: *Examination.* Trenton, Jan. 20-23. Sec., Dr. Royal A. Schaaf, 28 W. State St., Trenton.

NEW MEXICO:* *Examination and Reciprocity.* Sante Fe, May 18-19. Sec., Dr. R. C. Derbyshire, 227 East Palace Ave., Santa Fe.

NORTH CAROLINA: *Reciprocity.* Southern Pines, Jan. 17. *Examination.* June. Asst. Sec., Mrs. Louise J. McNeill, 716 Professional Bldg., Raleigh.

NORTH DAKOTA: *Examination and Reciprocity.* Grand Forks, Jan. 7-10. Sec., Dr. C. J. Glaspel, Grafton.

OKLAHOMA:* *Examination.* Oklahoma City, June 2-3. Exec. Sec., Mrs. E. L. Haidek, 813 Braniff Bldg., Oklahoma City.

PUERTO RICO: *Examination and Reciprocity.* San Juan, March 3. Acting Secretary, Dr. Herminio Mendez Herrera, Box 9156, Santurce.

SOUTH DAKOTA:* *Examination.* Sioux Falls, Jan. 20-21. Exec. Sec., Mr. John C. Foster, 300 First National Bank Bldg., Sioux Falls.

UTAH: *Examination.* Salt Lake City, July 8-10. Dir., Mr. Frank E. Lees, 324 State Capitol Bldg., Salt Lake City 1.

WASHINGTON:* *Examination.* Seattle, Jan. 12-14. Sec., Mr. Thomas A. Carter, Capitol Bldg., Olympia.

WISCONSIN:* *Examination and Reciprocity.* Madison, Jan. 13-15. Sec., Dr. Thomas W. Tormey, Jr., 1140 State Office Bldg., 1 West Wilson St., Madison.

WYOMING: *Examination and Reciprocity.* Cheyenne, Feb. 2. Sec., Dr. Franklin D. Yoder, State Office Bldg., Cheyenne.

BOARDS OF EXAMINERS IN THE BASIC SCIENCES

ARKANSAS: *Examination.* Little Rock, May 4-5. Sec., Dr. S. C. Dellinger, University of Arkansas, Fayetteville.

CONNECTICUT: *Examination.* New Haven, Feb. 14. Exec. Asst., Mrs. Regina G. Brown, 258 Bradley St., New Haven 10.

FLORIDA: *Examination.* Miami, June 6. Sec., Mr. M. W. Emmel, University of Florida, Box 340, Gainesville.

IOWA: *Examination.* Des Moines, Jan. 13. Sec., Dr. Elmer W. Hertel, Wartburg College, Waverly.

KANSAS: *Examination.* Kansas City, June. Sec., Dr. L. C. Heckert, Pittsburg.

MICHIGAN: *Examination.* Ann Arbor and Detroit, Feb. 12-13. Sec., Mrs. Anne Baker, 116 Stevens T. Mason Bldg., West Michigan Ave., Lansing.

NEW MEXICO: *Examination.* Santa Fe, Jan. 18. Sec., Mrs. Marguerite Cantrell, Box 1522, Santa Fe.

OKLAHOMA: *Examination.* Oklahoma City, Mar. 27-28. Exec. Sec., Mrs. L. Haidek, 813 Braniff Bldg., Oklahoma City.

RHODE ISLAND: *Examination.* Providence, Feb. 18. Administrator of Professional Regulation, Mr. Thomas B. Casey, 366 State Office Bldg., Providence.

TEXAS: *Examination.* April 1959. Certificates issued by reciprocity and waiver on the first and fifteenth of each month. Sec., Bro. Raphael Wilson, 407 Perry-Brooks Bldg., Austin.

*Basic Science Certificate required.

GOVERNMENT SERVICES

DEFENSE DEPARTMENT

Forensic Pathology Registry.—A Registry of Forensic Pathology has been established at the Armed Forces Institute of Pathology, Washington, D. C. It will be the 24th component of the American Registry of Pathology, and it is under the sponsorship of the College of American Pathologists. The objective of the new registry is the collection of well-checked and well-documented medicolegal cases to be used as a reservoir for teaching and research. Only selected cases of medicolegal interest contributed by a qualified pathologist will be registered. The material will be incorporated in the files of the Armed Forces Institute of Pathology and become a part of its national collection of pathology.

Registry consultation on contributed cases will be limited to basic pathological changes and will not include medicolegal opinions which might involve Armed Forces Institute of Pathology staff members in court proceedings. Cases are now being accepted for registration. A six-month fellowship in forensic pathology at the Armed Forces Institute of Pathology has been provided by the college as a part of its sponsoring support.

Aviation Pathology Committee Elects New Officers.—Officers for 1959 have been elected by the Joint Committee on Aviation Pathology, which held its fifth business meeting in December at the Armed Forces Institute of Pathology. They are Capt. Carl E. Wilbur, M. C., U. S. Navy, chairman, and Capt. Murray W. Ballenger, M. C., U. S. Navy, secretary. The committee, which includes medical officers of the military services of the United States, the United Kingdom, and Canada, uses the institute as the central coordinating facility for investigating the pathology of fatal aircraft accidents. Captain Wilbur, who is head of the Aviation Medicine Safety and Flight Training Branch, Bureau of Medicine and Surgery, Navy Department, Washington, D. C., will replace Col. Frank M. Townsend, M. C., U. S. Air Force deputy director of AFIP, as chairman. Captain Ballenger, who is on duty at the Armed Forces Institute of Pathology, will replace as secretary another staff member, Fathollah K. Mostofi, M. D., scientific director of the American Registry of Pathology.

AIR FORCE

Consultants Visit Medical Installations Abroad.—Drs. Garfield G. Duncan and Edgar J. Poth, national consultants to the Air Force surgeon general, recently visited medical installations in Germany, France, England, and Spain. They provided advice on problem cases in their respective specialities and conducted lectures and teaching sessions at medical installations. Doctor Duncan, of the Pennsylvania Hospital in Philadelphia, is a national consultant in internal medicine, and Doctor Poth, of the University of Texas Medical Branch in Galveston, is a national consultant in surgery.

VETERANS ADMINISTRATION

New Hospital Building at Fort Meade.—The VA Hospital at Fort Meade, S. D., occupies a new 60-bed combined medical, surgical, and administrative building Dec. 8, 1958. Fort Meade is a 720-bed neuropsychiatric hospital located 30 miles north of Rapid City on the site of a former U. S. Cavalry Post established soon after the Battle of the Little Bighorn. Fort Meade was garrisoned by Gen. George Custer's former regiment, the Fourth

New hospital at Fort Meade, S. D.

Cavalry, for many years. The new hospital building which provides beds for psychiatric patients with acute medical and surgical problems is the first phase of a long range construction program which will eventually replace all present bed facilities now housed in converted Army barracks.

PUBLIC HEALTH SERVICE

Multiple Sclerosis Leaflet.—Recent developments in research on multiple sclerosis are described in a leaflet entitled "Multiple Sclerosis—Hope Through Research." One of the recent advances reported in the leaflet is a new understanding of myelin through biochemical research. Scientists have now discovered the specific manner in which one of the essential compounds of myelin, sphingosphine, is formed in the body and are now able to produce this substance in the laboratory. This new development may lead to additional knowledge concerning the disappearance of myelin and the possible reversal of this process. Prepared by the National Institute of Neurological Diseases and Blindness, National Institutes of Health, the leaflet is listed as Public Health Service publication no. 621 and Health Information series no. 92. Single free copies may be obtained from the National Institute of Neurological Diseases and Blindness, Bethesda 14, Md. The leaflet may be purchased in quantity from the Superintendent of Documents, Government Printing Office, Washington 25, D. C., at $3 for 100 copies.

DEATHS

Angeloni, Tito Ⓜ Providence, R. I.; Regia Università di Napoli Facoltà di Medicina e Chirurgia, Italy, 1905; died in Rocchetta al Volturno, Italy, Oct. 10, aged 79.

Bachulus, Matthew John Ⓜ Springfield, Mass.; Harvard Medical School, Boston, 1932; fellow of the American College of Surgeons; on the courtesy staff, Wesson Memorial Hospital; served on the staffs of the Westfield (Mass.) State Sanatorium, and the Springfield Hospital, where he died Oct. 27, aged 56.

Baxter, Harry Toler Ⓜ Astoria, Ill.; University of Illinois College of Medicine, Chicago, 1914; died in the Graham Hospital, Canton, Oct. 14, aged 66.

Becker, Charles Frederick Ⓜ Camden, N. J.; Jefferson Medical College of Philadelphia, 1953; member of the staff of Cooper Hospital; found dead in bed Oct. 28, aged 33.

Bellantoni, Raphael, Tuckahoe, N. Y.; Long Island College Hospital, Brooklyn, 1924; fellow of the American College of Surgeons; an associate member of the American Medical Association; director of obstetrics at the Union Hospital in New York City; consultant at the St. Joseph's Hospital in Yonkers and the Harlem Hospital in New York City; died Oct. 28, aged 59.

Blauvelt, John Hudson, Nyack, N. Y.; Cornell University Medical College, New York City, 1911; member of the American Psychiatric Association and the Industrial Medical Association; served on the staff of the Matteawan State Hospital in Beacon; died Oct. 31, aged 69.

Braun, Robert Frederick, Wausau, Wis.; Marquette University School of Medicine, Milwaukee, 1915; veteran of World War I; died Oct. 13, aged 74.

Broughton, George Anthony, La Jolla, Calif.; Medical Department of the University of California, San Francisco, 1896; an associate member of the American Medical Association; fellow of the American College of Surgeons; died Oct. 20, aged 83.

Bryan, Charles Silas Jr. Ⓜ Oakland, Calif.; Harvard Medical School, Boston, 1937; certified by the National Board of Medical Examiners; specialist certified by the American Board of Radiology; member of the American College of Radiology; veteran of World War II; clinical instructor of radiology at Stanford University School of Medicine in San Francisco; formerly on the staff of the Truesdale Hospital in Fall River, Mass.; associate radiologist at the Peralta Hospital; died Oct. 28, aged 47.

Burner, George Washington, Johnstown, Ohio; Columbus Medical College, 1892; veteran of World War I; for 10 years postmaster at Johnstown; died in Marysville Oct. 15, aged 95.

Carman, James Edwin, La Canada, Calif.; University of Minnesota College of Medicine and Surgery, Minneapolis, 1901; for many years practiced in Detroit Lakes, Minn.; died in the Elwood Sanitarium in Pasadena, Oct. 17, aged 80.

Crawford, William Shell, Tulsa, Okla.; Medical College of South Carolina, Charleston, 1914; served as a captain in the medical corps of the U. S. Army; for 26 years medical director of the Carter Oil Company; died Oct. 15, aged 67.

Deal, William Floyd Ⓜ Craig, Colo.; University of Nebraska College of Medicine, Omaha, 1919; on the staffs of St. Luke's Hospital in Denver and Memorial Hospital; died Oct. 22, aged 65.

Derr, John Sebastian Ⓜ Frederick, Md.; University of Virginia Department of Medicine, Charlottesville, 1905; specialist certified by the American Board of Radiology; fellow of the American College of Physicians; member of the American Roentgen Ray Society, Radiological Society of North America, and the American College of Radiology; from 1906 to 1908 a medical missionary in British West Africa; veteran of World War I; died Oct. 23, aged 77.

Dodd, Wilson Farnsworth Ⓜ Pleasant Hill, Tenn.; Cornell University Medical College, New York City, 1920; fellow of the American College of Surgeons; for many years a medical missionary in Turkey; during World War II was appointed medical director of the Near East Foundation in Greece; formerly medical director of the Berea (Ky.) College; on the staff of the Uplands Cumberland Mountain Sanatorium; died Oct. 30, aged 65.

Duncan, Owsley Bennett Ⓜ Paterson, N. J.; Columbia University College of Physicians and Surgeons, New York City, 1904; veteran of World War I; on the staff of the Barnert Memorial Hospital; died Oct. 15, aged 81.

Edwards, Aaron Robinson Ⓜ Ann Arbor, Mich.; Cornell University Medical College, New York City, 1938; interned at the Harper Hospital in Detroit; served a residency at the Children's Hospital

Ⓜ Indicates Member of the American Medical Association.

in Detroit and the University Hospital in Ann Arbor, Mich.; specialist certified by the American Board of Pediatrics; member of the American Academy of Pediatrics; veteran of World War II; on the staffs of the Beyer Memorial Hospital, Ypsilanti, and St. Joseph Mercy Hospital; aged 46; died Nov. 9.

Franklin, Samuel Nathan Ⓜ West Allis, Wis.; Marquette University School of Medicine, Milwaukee, 1916; formerly county coroner; died in the Mount Sinai Hospital Oct. 14, aged 76.

Frost, Horace Bird, Lavonia, Ga.; Harvard Medical School, Boston, 1896; died in the Stephens County Hospital, Toccoa, Oct. 18, aged 87.

Gale, Eugene Manson, Merrimac, Mass.; College of Physicians and Surgeons, Boston, 1914; member of the Massachusetts Medical Society; served in France during World War I; on the staff of the Amesbury (Mass.) Hospital, where he died Oct. 23, aged 67.

Geraghty, Francis Joseph Ⓜ Baltimore; University of Maryland School of Medicine and College of Physicians and Surgeons, Baltimore, 1926; assistant professor of medicine at his alma mater; specialist certified by the American Board of Internal Medicine; fellow of the American College of Physicians; past-president of the Baltimore City Medical Society, of which he was a member of the executive committee; president of the staff and chief of medicine at the Bon Secours Hospital; on the staffs of the Mercy, Union Memorial, and University hospitals; died Nov. 1, aged 60.

Goldrick, Harold, New York City; University of Kazan Faculty of Medicine, Russia, 1919; on the staff of the New York Polyclinic Medical School and Hospital; died Oct. 26, aged 65.

Goodrich, Joseph Albert, Glenwood, Iowa; Northwestern University Medical School, Chicago, 1905; died Oct. 13, aged 85.

Guthrie, Donald Ⓜ Sayre, Pa.; born in Wilkes-Barre, June 23, 1880; University of Pennsylvania Department of Medicine, Philadelphia, 1905; emeritus professor of clinical surgery at the University of Pennsylvania Graduate School of Medicine in Philadelphia; professor, division of surgery, Hahnemann Medical College and Hospital of Philadelphia; gave the Ernest A. Sommer Memorial Lecture in Portland, Ore., in 1941 and the Mayo Lecture, University of Michigan, Ann Arbor, in 1954; in 1932 member of the House of Delegates of the American Medical Association; past-president of the Medical Society of the State of Pennsylvania, of which he was a councilor and trustee; past-president of the Alumni Association of the Mayo Foundation, Bradford County Medical Society, and the New York and New England Railroad Surgeons; member of the American Surgical Association, Surgical Research Society, Southern Surgical Association, American Association for the Surgery of Trauma, International Society of Surgeons, Royal Academy of Medicine, Rome, Conference, Board of Physicians in Industry, American Goiter Association, Royal Medical Society, Budapest, and the Association of Railroad Chief Surgeons; honorary member of the Society of Medicine and Surgery, Rio de Janeiro; fellow, and from 1930 to 1952 a member of the board of governors of the American College of Surgeons; member of the founders group of the American Board of Surgery; in 1937 received the honorary doctor of science degree from the Lafayette College, Easton, Pa.; on June 14, 1956, at the 109th annual commencement exercises of the Hahnemann Medical College and Hospital of Philadelphia, was awarded the honorary degree of doctor of humane letters; received an alumni award of merit in January of this year from the General Alumni Society of the University of Pennsylvania in recognition of outstanding service to the university; member of the surgical staff, Mayo Clinic, Rochester, Minn., from 1906 to 1909; served on the advisory board, *American Journal of Surgery;* for many years chief surgeon of the Lehigh Valley Railroad; founder of the Guthrie Clinic and chief surgeon of Robert Packer Hospital, where he died Oct. 30, aged 78.

Heck, Charles Christian Ⓜ Syracuse, N. Y.; University of Rochester School of Medicine and Dentistry, Rochester, N. Y., 1933; member of the Industrial Medical Association; veteran of World War II; physician for the state athletic commission; served as medical director of the Syracuse University athletic department; member of the staff of St. Joseph's Hospital, where he served an internship; died Oct. 30, aged 54.

Hedrick, Thomas Wade Ⓜ Abilene, Texas; University of Texas School of Medicine, Galveston, 1916; fellow of the American College of Surgeons; on the staffs of St. Ann Hospital, Cox Memorial Hospital, and the Hendrick Memorial Hospital, where he died Oct. 21, aged 67.

Hillis, Albert Edward Ⓜ Tacoma, Wash.; University of Michigan Department of Medicine and Surgery, Ann Arbor, 1902; specialist certified by the American Board of Otolaryngology; fellow of the American College of Surgeons; past-president of the Pierce County Medical Society; on the staff of the Northern Pacific Beneficial Association; charter member of the Tacoma Lions Club; died in South Pasadena, Calif., Oct. 24, aged 84.

Horstman, Frank Marion, Northbrook, Ill.; College of Physicians and Surgeons of Chicago, School of Medicine of the University of Illinois, 1904; also a graduate in pharmacy; formerly on the faculty of his alma mater and the Loyola University School

of Medicine in Chicago, where he served as a member of the council; for many years on the staff of the McKinley High School in Chicago; for three years an examining physician for the Chicago, Burlington, and Quincy Railroad; formerly associated with the Augustana Hospital in Chicago; died Oct. 27, aged 80.

Huey, William, Seattle; University of Edinburgh Faculty of Medicine, Scotland, 1939; died Oct. 24, aged 45.

Hutchinson, Claribel Merrill, Pasadena, Calif.; Woman's Medical College of the New York Infirmary for Women and Children, New York City, 1887; died Oct. 26, aged 100.

Jeppson, John Rufus Ⓜ New Rochelle, N. Y.; Jefferson Medical College of Philadelphia, 1923; on the staff of the New Rochelle Hospital; died Nov. 2, aged 62.

Jones, Milton Easley Ⓜ Ocean City, Md.; University of Maryland School of Medicine and College of Physicians and Surgeons, Baltimore, 1915; member of the American Urological Association and the Ohio State Medical Association; formerly practiced in Columbus, Ohio, where he was associated with Mount Carmel and Grant hospitals; died in the Peninsula General Hospital, Salisbury, Oct. 21, aged 70.

Kinnamon, Frank Ⓜ Concordia, Kan.; Kansas Medical College, Medical Department of Washburn College, Topeka, 1912; county coroner and health officer; for 12 years member of the board of education; on the staff of St. Joseph's Hospital, where he died Oct. 9, aged 78.

Kohler, Delphin William Ⓜ Tacoma, Wash.; John A. Creighton Medical College, Omaha, 1916; member of the American Academy of General Practice; service member of the American Medical Association; veteran of World War I; retired from the Veterans Administration Aug. 1, 1955; formerly on the staff of the Veterans Administration Hospital in American Lake; died Oct. 28, aged 70.

Kolettis, George John Ⓜ Gary, Ind.; National University of Athens School of Medicine, Greece, 1915; died in St. Mary's Mercy Hospital Aug. 27, aged 64.

Lahn, Louis Ⓜ Great Neck, N. Y.; born in Norwich, Conn., Aug. 22, 1895; Fordham University School of Medicine, New York City, 1921; specialist certified by the American Board of Obstetrics and Gynecology; adjunct professor of gynecology and obstetrics at the New York Polyclinic Medical School and Hospital; associate in obstetrics and gynecology at the New York Medical College, Flower and Fifth Avenue Hospitals; fellow of the American College of Surgeons and the International College of Surgeons; practiced in New York City, where he was associated with the Flower and Fifth Avenue Hospitals, Hospital for Joint Diseases, Metropolitan Hospital, and the Bird S. Coler Hospital; died in the William W. Backus Hospital, Norwich, Conn., Oct. 30, aged 63.

Lape, Charles Pearley, Buffalo; Hahnemann Medical College and Hospital of Philadelphia, 1909; member of the Medical Society of the State of New York; specialist certified by the American Board of Radiology; a charter member of the Buffalo Radiological Society; served on the staff of the Millard Fillmore Hospital; died in Portland, Maine, Oct. 13, aged 75.

MacLiesh, Henry, Brooklyn; Medizinische Fakultät der Universität, Vienna, Austria, 1925; on the staff of the Unity Hospital and Adelphi Hospital; died in the Mount Sinai Hospital, New York City, Aug. 3, aged 57.

McCuskey, John Fulton Ⓜ Clarksburg, W. Va.; born in Hingham, Mass., April 6, 1910; Northwestern University Medical School, Chicago, 1937; specialist certified by the American Board of Urology; member of the American Urological Association and the Southern Medical Association; from 1953 to 1956 a member of the council of the West Virginia State Medical Association; fellow of the American College of Surgeons; past-president and secretary of the Harrison County Medical Society; during World War II was assigned to the 106th Station Hospital and served in Italy, Okinawa, and Japan; released from the service in 1946 with the rank of lieutenant colonel; past-president of the staffs of St. Mary's and Union Protestant hospitals; aged 48; died Oct. 30.

Marra, Frank Paul Ⓜ Schenectady, N. Y.; Albany (N. Y.) Medical College, 1927; member of the American Academy of General Practice; served as city councilman; died Oct. 25, aged 54.

Monroe, Alvin Henry, Elmira, N. Y.; Syracuse University College of Medicine, 1909; an associate member of the American Medical Association; served as medical examiner for the Chemung County Draft Board during World Wars I and II and served as health officer for the town of Southport; for many years county coroner; associated with the Arnot Ogden and St. Joseph's hospitals; died Oct. 23, aged 77.

O'Malley, William P., Milwaukee; University of Wisconsin Medical School, Madison, 1928; member of the American Academy of General Practice; veteran of World War I; past-president of the Wauwatosa Kiwanis Club; on the staff of the Milwaukee Hospital; died Oct. 28, aged 60.

Op de Beeck, Fernand G. P., Montvale, N. J.; Universteit Gent Faculteit der Geneeskunde, Belgium, 1902; died Sept. 3, aged 83.

Ostfield, E. Vaughn, Pittsburgh; University of Pittsburgh School of Medicine, 1958; intern at the Presbyterian Hospital; found dead at her summer cottage near Confluence Dam, Sept. 28, aged 29.

Paul, Robert Clifford Ⓜ Wooster, Ohio; University of Wooster Medical Department, Cleveland, 1892; served on the draft board during World Wars I and II; past-president and secretary of the Wayne County Medical Society; on the staff of the Wooster Community Hospital; died Oct. 28, aged 97.

Powers, Edward Sharp Ⓜ North Hollywood, Calif.; Washington University School of Medicine, St. Louis, 1935; veteran of World War II; associated with St. Joseph Hospital in Burbank and the Good Samaritan Hospital in Los Angeles; died at the International Airport in Inglewood Oct. 23, aged 50, while awaiting a plane for a vacation trip to Mexico.

Robison, E. Waid, Dallas, Texas; Baylor University College of Medicine, Dallas, 1926; veteran of World War II; served on the staffs of the Veterans Administration hospitals in Waco and Bonham; associated with the Taylor Clinic; aged 59; died Oct. 8.

Schauffler, Robert McEwen Ⓜ Kansas City, Mo.; Columbia University College of Physicians and Surgeons, New York City, 1896; formerly on the faculty of the University of Kansas School of Medicine in Kansas City, Kan.; past-president of the Jackson County Medical Society; member of the American Orthopaedic Association, Clinical Orthopaedic Society, and the American Academy of Orthopaedic Surgeons; fellow of the American College of Surgeons; for many years on the staff of the Children's Mercy Hospital; died in the Research Hospital Oct. 30, aged 87.

Seibert, Daniel Glenn, Jackson, Mo.; Vanderbilt University School of Medicine, Nashville, Tenn., 1901; for many years on the school board; died in the Southeast Missouri Hospital, Cape Girardeau, Oct. 3, aged 81.

Smith, Thomas Elmo Ⓜ Independence, Kan.; Kansas City (Mo.) Medical College, 1904; served as a member of the state legislature; vice-president and director of the Independence State Bank; on the staff of the Mercy Hospital, where he died Oct. 21, aged 80.

Sturdivant, Burton Barrett, West Union, W. Va.; Maryland Medical College, Baltimore, 1912; county health officer; during World War I was a member of the medical corps of the U. S. Army and served overseas as regimental surgeon of the 540th engineers with the rank of captain; died in Winston–Salem, N. C., Oct. 31, aged 71.

Van Arsdall, Condit Brewer Ⓜ Harrodsburg, Ky.; Johns Hopkins University School of Medicine, Baltimore, 1902; for many years served on the board of education and 14 years as chairman; served as president and secretary of Mercer County Medical Society; for many years president of the Harrodsburg Historical Society; served eight years as a member of the board of directors of the Good Samaritan Hospital in Lexington; member of the staff and board of trustees of the James B. Haggin Memorial Hospital, where he died Oct. 25, aged 83.

Whetstone, Adair K. Ⓜ Sylacauga, Ala.; Birmingham Medical College, 1914; received the Good Citizenship citation of the Civitan Club; voted "Man of the Year" by the Chamber of Commerce; on Aug. 2, 1953, Sylacauga observed "Dr. Whetstone Day" to pay tribute to him for his service to this section; church services as well as a city-wide afternoon meeting honored him and at that time three Dr. Whetstone Scholarships were established for the Sylacauga Hospital School of Nursing; on the staffs of the Drummond Fraser Hospital and the Sylacauga Hospital, where he died Oct. 19, aged 80.

Wilson, Harry Franklin Ⓜ Columbia, S. C.; born in Bowman Aug. 23, 1904; Medical College of South Carolina, Charleston, 1928; veteran of World War II and was awarded the American Defense, Armed Forces Reserve, American Theater, Asiatic–Pacific Theater with two battle stars, Victory, Occupational (Japan), and the Philippine Liberation campaign ribbons for Army service; in 1951 was awarded the Cross of Military Service of the United Daughters of the Confederacy; since 1949 director of the division of laboratories of the state health department and formerly served as director of industrial health; formerly health officer of Horry County, Beaufort County, and the Dillon–Marion Health District; died in the Veterans Administration Hospital Oct. 23, aged 54.

Woodcock, Lee Barnes, Sedona, Ariz.; Medico-Chirurgical College of Philadelphia, 1898; died Oct. 24, aged 87.

Woods, Ernest Arthur Ⓜ Ashland, Ore.; University of Minnesota College of Medicine and Surgery, Minneapolis, 1899; specialist certified by the American Board of Otolaryngology; past-president and secretary of the Southern Oregon Medical Society; past-president of the Jackson County Medical Society; formerly member of the council of the Oregon State Medical Society; served as a member of the city council; company surgeon for Southern Pacific Railroad; served on the staff of the Community Hospital; died Oct. 12, aged 83.

Wylie, Robert Lawson Ⓜ Scotts Hill, Tenn.; University of Tennessee Medical Department, Nashville, 1906; for 46 years president of the Farmers State Bank; on Oct. 14, 1950, honored on "Dr. Wylie Day" and his friends presented him with a new automobile; died Oct. 11, aged 81.

FOREIGN LETTERS

AUSTRIA

Iron-Deficiency Anemia.—At the meeting of the Society of Physicians in Vienna on Nov. 7, Drs. A. Stacher and J. Böhnel said that iron tablets do not always agree with the patients and are not always absorbed properly. Intravenous injections sometimes cause thrombosis and other side-effects. They treated a series of 47 patients, of whom 17 had essential hypochromic anemia, 16 posthemorrhagic anemia, 9 anemia caused by infection and tumors, and 5 postoperative anemia with intramuscularly administered iron-dextran complex (Myofer) and found that the hematopoietic effect of the drug was equal to that of intravenous injections. These results were corroborated in some patients by constant control of the iron content in the serum. In patients with anemia caused by infections or tumors in whom no concomitant true iron-deficiency due to hemorrhages was present, no significant improvement could be achieved while the other types of iron-deficiency anemia showed excellent remissions with the intramuscular treatment.

Treatment of Neuralgia.—A the same meeting Dr. F. Bodart reported on a series of 28 patients with neuralgia due to involvement of nerve roots, chiefly sciatica, whom he treated with intrathecal injections of prednisolone. Nine of the patients became free from pain and remained so. In the rest the reaction was of short duration. Meningism as a side-effect sometimes occurred. This treatment was considered a valuable addition to the measures hitherto used.

Dissemination in the Course of Eczema.—At the same meeting Dr. W. Lindemayr reported on the clinical aspect and the course of the dissemination reaction observed in 100 patients with generalized eczema which had spread from an initially circumscribed lesion. On the basis of intracutaneous and epicutaneous tests with bacterial and fungus allergens and epicutaneous tests with contact allergens which possibly have an additional effect, the speaker concluded that the dissemination reactions should be ascribed to an allergy against autoantigens. The evidence indicates that these autoantigens develop in the primary focus under the influence of bacteria and fungi.

Anemia and Geophagia.—At the meeting of the Society of Physicians in Vienna on Nov. 14, Dr. H. G. Weippl said that geophagia has long been of interest only to the psychiatrist, but it is coming to be of interest to roentgenologists and pediatric hematologists as well. Four children, their ages ranging from 1 to 2 years, with geophagia and severe hypochromic anemia were observed. Thorough examination, especially of the serum iron level, revealed iron-deficiency as the cause of the anemia. When geophagia was no longer present and the children were given iron therapy, immediate improvement of the anemia was noted. Even without iron therapy a gradual improvement could be seen. The obsessive eating of abnormal objects is rare in Europe, and the geophagia in children of this age is considered a benign, temporary disturbance which does not reflect a disturbed mental development.

BRAZIL

Diagnosis of Syphilis.—At the meeting of the São Lucas Medical Society of São Paulo in October, Dr. Luiz Migliano reported that a series of 523 positive Migliano microreactions agreed with the results of the standard and presumptive Kahn test on the same serums, and a series of 16,761 negative reactions agreed with the results of Kahn, Meinik, and Wassermann tests. The simplicity of the technique of the Migliano's reaction and the fact that a minimum of material is necessary for its performance makes it of great use for routine examinations.

Operations for Pelvic Cancer.—Dr. Azael Leistner (*Revista de medicina e cirurgia de São Paulo*, July, 1958) performed 15 pelvic exenterations (10 total and 5 partial) for carcinoma of the uterine cervix, vulva, rectum, and bladder, with local metastases to the lymph nodes. Most of the patients had been previously operated on or had received roentgen and radium therapy with unsatisfactory results. Dr. Leistner made 13 temporary cutaneous ureterostomies (he does not advise ureterosigmoidostomies because of the danger of stenosis, infection, and acidosis), 2 ileocecal bladder reconstructions, and 1 ureteroileosigmoidostomy, which should be performed in patients in whom the cancer is supposedly cured. The total volume of whole blood used during the operation was from 1.5 to 3.8 liters. In one patient he suspended the bladder and made the abdominopelvic separation with a graft of the fascia lata, with excellent results. In another, he peritonealized the pelvis suturing the anterior parietal peritoneum to the posterior peritoneum. There were five deaths in the late postoperative period

(3rd, 4th, 5th, and 10th months) and seven in the immediate postoperative period. One patient was in good condition when last seen 6 months after operation and another 23 months after operation. The adverse results were probably due to the fact that in many cases the operation was done for palliative reasons (in patients with urinary and fecal fistulas). The author believed that the operation should be done only when there is adequate equipment and a well-trained surgical staff.

Surgical Treatment of Goiter.—Dr. R. A. Santos (*Revista paulista de medicina*, vol. 53, 1958) operated on 303 patients with thyroid diseases; 185 (61.1%) with simple goiter, 110 (36.3%) with toxic goiter, 4 (1.3%) with tuberculous thyroiditis, and 4 with other conditions. Of the 50 patients whose basal metabolism was determined, in 33 with diffuse toxic goiter the metabolic rate averaged 128, and in 17 with nodular toxic goiter the rate averaged 130. The patients with diffuse goiter presented the highest and the lowest increases in metabolic rate, since the hyperthyroidism of this type of goiter responds rapidly to chemical treatment and several patients had undergone previous medical treatment with iodine. Further spontaneous remissions may occur.

In the 110 patients with toxic goiter, 111 operations were performed. There were three deaths, or a fatality rate of 2.7%, and several patients presented complications. Three suffered a thyrotoxic crisis in the immediate postoperative period. One of these patients who had been operated on before the introduction of the hibernotherapy died, and another, treated by hibernation, recovered promptly from a thyrotoxic crisis. The third patient of this group died a few hours after operation. Tetany occurred in only one patient (on the fifth day after the operation), the crisis having been successfully treated with only calcium and vitamin D. The author believes that, as a rule, no other drugs are needed. Chvostek's and Trousseau's signs were not looked for, the first being almost always present in the first days after operation and therefore without special significance. Hyperthyroidism in the last postoperative period occurred in four patients, one of whom had uncontrollable vomiting. Hyperthyroidism was much less frequent in patients with simple goiter—one case in the 185 patients. There was no case of aggravation of exophthalmus after the operation, but a few patients had slight hemorrhages.

Plastic Surgery of the Esophagus.—Dr. O. M. Dantas reported to the Associacão Paulista de Medicina a series of 16 patients with cancer of the esophagus in whom a total reconstruction of the organ was performed in 15 by using a portion of the colon and in one by using a portion of the stomach. In two patients whose tumor was situated in the lower third of the esophagus the route of access was a transdiaphragmatic thoracolaparotomy, but the author considers this a bad route, in view of the difficulties caused by the thoracopulmonary dynamics, mainly from the section of the diaphragm. From the technical standpoint this is a good route, as it widely exposes the lower third of the esophagus, permitting easy handling of the stomach and colon. For total esophagectomy, however, this route is unsuitable, since the separation of the esophagus at the level of and above the aortic arc causes dangerous reflexes. The placing of the colon in the thoracic cavity reduces the pulmonary capacity and causes compression of the left bronchus, hindering the elimination of secretions and favoring the occurrence of atelectasis. Too long an exposure of the pleural cavity with the lung collapsed favors the occurrence of pulmonary complications. These reasons led the author to abandon this route.

In three patients whose tumor was situated on the middle third of the esophagus, the operation was performed in two stages. In the first, a right thoracotomy, esophagectomy, closure of the thoracotomy, left laparotomy, distal section of the esophagus, gastrostomy, and cervical esophagostomy were accomplished. In the second a laparotomy for the closure of the gastrostomy, cologastroanastomosis, and left thoracotomy for the interposition of the colon with cervical colostomy were performed. As the interposition of the colon through the hemithorax was considered inconvenient, the author tunnelized the anterior mediastinum for the interposition of the colon. He believed that by this procedure the colon or the stomach, when placed in the anterior mediastinum, did not interfere with the function of the heart and the large vessels and was more easily tolerated by the lungs than when placed in the thoracic cavity. All the patients on whom this route was used had an uneventful postoperative course. The experience of the author with the mediastinal tunnelization led to its use for all esophageal tumors. It was even possible in several patients to perform the operation in one stage. From the point of view of the route of access, the author recommends tunnelization for the reconstruction of the esophagus. As complications of this procedure, abscess of the mediastinum, due to insufficient length of the colon and obstruction by compression of the colon against the sternal manubrium, were observed.

Labor After Previous Cesarean Section.—Dr. Martiniano Fernandes (*Revista de ginecologia e d'obstetricia*, vol. 52, 1958) reported a series of 1,515 deliveries by cesarean section. Of these, 210 patients had had a previous cesarean section and in 33 a trial of natural delivery resulted in dehiscence of the uterine scar. The good results of the transpelvic spontaneous deliveries observed in about 33% of the author's patients indicated the possibili-

ties of a trial at labor provided the patients are carefully selected. Contraindications of such a test may be ascertained by hysterography performed four months after cesarean section to discover faults in the scar. As most of the patients in this series presented obstetrical emergencies, the maternal death rate was 15% and the fetal death rate was 39.3%. The following conditions should be fulfilled for the best treatment of such patients: (1) roentgenographic proof of fetopelvic compatibility, (2) an easily dilatable cervix, (3) vertex presentation, (4) engagement of the head in the cervical canal, (5) normal uterine dynamics, and (6) absence of pain in the region of the surgical scar during the uterine contractions. In such patients the performance of version by external maneuvers, extractions, the application of forceps except at the end of the delivery, use of oxytocics, and Kristeller's maneuver are definitely contraindicated.

FRANCE

Coronary Arteriography.—At a meeting of l'Académie Nationale de Médecine, C. Arnulf of Lyon stated that he was able to inject a contrast medium into the ascending aorta during the cardiac pause induced by acetylcholine and lasting about nine seconds. By this means he obtained excellent roentgenograms of the coronary arteries first in experimental animals then in man without any untoward effects. This procedure is of value in localizing damage to the coronaries prior to surgical treatment.

Bronchogenic Cancer.—F. Denoix and co-workers (*Bulletin de l'association Française pour l'etude du cancer*, vol. 45, 1958) analyzed a series of 602 patients with bronchogenic cancer. They confirmed the existence of a correlation between these cancers and smoking. Other factors included chronic bronchitis, poor oral hygiene, inhalation of poisonous gas in World War I (even among nonsmokers), and heavy consumption of coffee. It is not yet known whether the benzopyrine in coffee is responsible for an increased incidence of lung cancer in coffee drinkers.

Respiratory Allergies in Children.—R. Mande and co-workers (*Annales de pédiatrie*, July, 1958) studied the allergenic action of house dust. Sensitivity to house dust was observed even in infants 6 months old. It was manifested by spasmodic or catarrhal rhinitis, fits of coughing, and typical asthmatic attacks. It was aggravated by tonsillectomy. An eosinophilia of 4 to 20% was observed and eosinophils were found in the bronchial secretions. In a series of 154 children treated by desensitizing injections, 1.9% were not benefited, 11.7% obtained partial improvement, and 86.4% were completely relieved.

Suppurative Adenitis due to BCG Vaccine.—R. Mande and co-workers (*La revue de la tuberculose*, vol. 3, 1958) found that in a series of 29,898 persons vaccinated with BCG vaccine, 96 developed suppurative adenitis, 48 of whom were less than 2 years old. The lesions appeared three months after vaccination; 26 involved more than one node. There were no severe reactions and recovery occurred in two or three months without treatment. In the children under 2 this complication was seen less frequently in those vaccinated by scarification than in those vaccinated by intradermal injection.

INDIA

Dementia Paralytica.—A. V. Rao (*Current Medical Practice*, vol. 2, September, 1958) reported that 33 (or 5%) of 661 consecutive new patients admitted to the Government Mental Hospital in Madras in 1954-1955 had dementia paralytica and in 1956 the incidence of this disease among new admissions was 3%. Among the 33 patients the highest age incidence was in the third and fourth decade; 2 patients were over 50 and 1 was only 20. Eleven of the patients had been mental workers and 11 had been manual laborers; 16 had pupillary abnormalities, in 8 of whom the typical Argyll Robertson pupil was seen while in 7 others incomplete Argyll Robertson pupils were noted. In one patient the pupils were dilated. Two had choroidoretinitis and two of the three patients with taboparesis had bilateral optic atrophy. Speech disturbances were present in 25 patients and consisted of slurring, anarthic mutism, nominal aphasia, palilalia, and echolalia. Twenty two of the patients had tremor of the tongue; 23 had tremor of the fingers; 4 developed convulsions; and hemiplegia was observed in 3. Associated tabes dorsalis was seen in three who also had Argyll Robertson pupils. Aural hematomas were seen in four patients. One had marked clubbing of the fingers in both hands. Two had spontaneous fractures involving both femurs due to osteoporosis and some had loss of weight. Only 11 had grandiose ideas and only 2 of these showed expansive megalomania. The simple demented type was seen in another 11; 5 showed acute maniacal excitement; 3 had chronic excitement; 2 showed depression; and 1 had auditory hallucinations. Loss of memory was common and so was insomnia. Four patients had Korsakoff's psychosis. Enlargement of the aortic shadow was seen in the chest roentgenograms of five patients. One had clinically recognizable aortic regurgitation and another had aneurysm of the ascending aorta. The spinal fluid gave a positive Wassermann reaction with a paretic type of colloidal gold curve in all patients. The blood and spinal fluid were serologically positive in 25.

UNITED KINGDOM

The Mind and the Machine.—The Nuffield Foundation has made a grant of $95,200 to the department of anatomy, University College, London, for the construction of a new computer which resembles the nervous system of an animal. This latest development in the study of the mind is based on the work of Prof. J. Z. Young on the learning mechanism of the octopus, which has remarkable ability to classify what it sees. Its skill in recognizing shapes depends on two sets of neurons that continually reactivate each other. If one set is put out of action, the octopus loses recent memories and only slowly learns any new classification, but its memory for old shapes is unaffected. It therefore seems that one of these sets forms the memory store, while the other is the printing device which inscribes new shapes on the memory. The arrangements by which the two parts are connected with each other have been worked out in detail. They involve several networks of nerve fibers, apparently a randomizing system allowing the possibility that each point in one lobe may be connected with any point in the next. It is to test these hypotheses that the new computer is to be built. It will consist of about 4,000 identical units, each of which will be an electronic analogue of a single neuron and its synaptic terminals. It is believed that in an animal information is stored at the synapses between neurons and that the receipt of nerve impulses changes the transmission power of the synapse. The units in the computer will be constructed to perform in the same way and thus give the computer a memory.

The networks will be trained to recognize shapes held in front of the computer's model eye. As each different shape is presented to the eye a different sound will be made in the machine's model ear. If the training is effective, the computer will be able to emit the appropriate sound when the shape is brought into its field of vision. It should also be within the range of the new computer to simulate the learning of the alphabet and the numerals and a limited number of more complex shapes which might even include human faces. The output stage will control the movement of levers that could simulate the movements of animals, the production of writing by man, or the generation of recognizable speech sounds. The computer should be finished by the end of 1960.

Trichomonal Vaginitis.—Of the compounds available for the local treatment of trichomonal vaginitis phenylmercuric dinaphthylmethane disulphonate is preferable to other preparations, being effective, free from toxic reactions, and acceptable to the patient, according to Murrell and Gray (*The Practitioner* **181**:611, 1958). This conclusion is based on their findings in a series of 125 patients, in 118 (94%) of whom the vagina was microscopically cleared of trichomonads at some stage during the trial. In 72 patients (60%) swabs from the vagina were negative for trichomonas after two weeks. Relapses or reinfestations occurred in 70 patients (56%) on at least one occasion: 29 (23%) of these patients defaulted at least once. Clinically, the end-results were classed as good in 97 patients (78%) and poor or failures in the rest. No intolerance or local sensitivity was encountered in any of the patients treated. In patients with heavy infestation, the vagina was swabbed under direct vision with an aqueous solution of the drug. The patients were instructed to insert two pessaries of the drug high in the vagina every night for two weeks, but to return in one week for progress to be assessed. In most patients treatment was continued with one pessary nightly for a further minimum period of four weeks, increasing to two pessaries at menstrual periods. Only those with a clinical urethritis accompanied by a positive urethral smear were given local treatment of the urethra: 60 ml. of a urethral jelly containing 0.1% of the drug, introduced by means of a tube fitted with a suitable nozzle. This procedure was repeated when necessary at subsequent visits.

Recurrent Stys.—Recurrent stys should be treated by an antibacterial ointment applied to both the nose and eyes, according to P. W. M. Copeman (*Lancet* **2**:728, 1958). This conclusion was based on the high incidence of Staphylococcus pyogenes var. aureus in the anterior nares of patients with recurrent stys. In a series of 18 patients with less than one sty a year, this organism was isolated from the nares in 8—an incidence of 44% of nasal carriers, which is similar to that in the general population. The comparable percentage in 36 patients with recurrent stys was 94. In most of these patients the application of a neomycin-bacitracin ointment to the nares was sufficient to break the run of stys, but in some it was also necessary to apply the ointment to the eyelids. It was therefore recommended that such an ointment be applied to the nares and the eyelids four times a day for 10 days, followed at biweekly intervals by courses of 7 days' treatment. This is frequent enough to prevent recolonization of the nares.

Physicians' Cathedral Window.—The Guildford division of the British Medical Association is appealing to the profession for contributions to a fund to provide one of the windows in the new Guildford cathedral, the nave of which is now nearing completion. It is believed that American physicians who served in or around Surrey in World War II may wish to participate in this gracious gesture. Donations should be sent to the Doctors' Cathedral Window Fund, c/o The Treasurer, Dr. F. A. Belam, 1 Westfield, Epsom Road, Guildford, Surrey.

MISCELLANY

REPORT ON CONFERENCE ON STAPHYLOCOCCIC DISEASE

The National Conference on Staphylococcal Disease, co-sponsored by the United States Public Health Service and the National Research Council, which met in Atlanta, Ga., headquarters of the Communicable Disease Center, Sept. 15-17, was attended by delegates from 59 professional organizations and numerous authorities on various aspects of the infection problem.

In the opening address, Dr. Leroy E. Burney, surgeon general of the Public Health Service, said that the purpose of the meeting was to review what is known about and to recommend what can be done to control staphylococcic infections which are acquired by hospital patients. These infections do not respond to the penicillin and other antibiotic drugs that kept them under control until recently.

The conference delegates agreed that the drug-resistant infection is now a problem in practically all hospitals throughout the world. Serious epidemics, although infrequent, have occurred unexpectedly in many hospitals.

Usually starting in surgical wards and in nurseries for newborn infants, the disease is spread through the hospital and out into the community by these patients, many of whom show no symptoms, such as boils and abscesses, until after they leave the hospital. Fear of causing public alarm which might deter persons from getting needed hospital care has caused some hospitals to attempt to hide their problem. However, hospital administrators who attended the conference reported a growing awareness that open recognition of the problem will contribute to its control.

Because staphylococcus germs are ubiquitous and because the drug-resistant strains permeate hospitals and their personnel, the prevention of serious infection, the delegates agreed, is a matter of finding how the dangerous strains are spread and building barriers against them. Although the delegates recognized that contaminated air and furnishings could be responsible for spreading the infection, the prevailing opinion was that personal contact is one of the most common causes. Most of their recommendations were therefore concerned with reducing this cause.

Their major recommendations included the following:

1. Organization of infection-control committees in all hospitals. These committees should have sufficient authority to investigate infections and establish and enforce hospital policies. They should include representatives from all services and divisions, all of whom should have a keen interest in the problem and should meet at regular and frequent intervals. Committee members should be responsible for seeing that hospital personnel are properly trained in anti-infection procedures and that these procedures are followed in daily activities. Local health officials should be asked to serve as consultants to these committees. The organization of infection-control committees by local medical societies, with representatives from the medical, nursing, and housekeeping staffs of all the hospitals in the area, was considered a necessary supplement to the intrahospital committee.

2. Use of an "infection log" in which all infections would be classified and pertinent data recorded. This would make it possible to determine whether infections are increasing and would also help the control committee to evaluate the effectiveness of its measures.

3. A plan for excluding from contact with patients all personnel who have boils or other active staphylococcic lesions or who are known to be carriers of dangerous and epidemic strains. Periodically, in nurseries for the newborn and at times of epidemics in other areas of the hospital, cultures should be made from personnel in order to detect, remove, and treat dangerous carriers. During epidemics, persons found to be carriers of dangerous epidemic strains should be removed from contact with patients until they are free from infection.

4. A local plan for establishing criteria for the discriminate use of antibiotics in medical and surgical treatment. Prophylactic use of antibiotics was considered highly undesirable.

5. Arrangements to store cultures from staphylococcic infections. This would help the hospital to trace the source of an epidemic if one should occur. The length of time these cultures should be stored would be decided by the infection-control committee.

6. Isolation of infectious patients, particularly those with pulmonary and skin infections, even if this means expanding isolation facilities. More emphasis on home care, in preference to hospitalization, was also suggested for patients with minor illnesses or with diseases that make them particularly vulnerable to staphylococcic infection. Diagnostic and treatment procedures in the hospital

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A symposium on staphylococcic infections was published in THE JOURNAL March 8, 1958, page 1177.

that open the skin—which is the normal barrier to staphylococcic infection—should be kept to a sensible minimum.

7. Special precautions in nurseries for newborn infants, such as elimination of overcrowding and maintenance of rigid sanitary standards. Bathing babies immediately after birth with an antiseptic such as hexachlorophene was also recommended. Since babies are the principal source of spreading the disease into the community, sample surveys of families at periodic intervals after their babies have been discharged from the hospital were advised. Such surveys can be made by telephone, mail questionnaire, or home visit. Early detection of nursery-acquired infection would help to prevent further spread. These surveys would also indicate whether the hospital had an infection problem which it had not recognized because of the late appearance of symptoms.

8. Development of intensive and continuous training programs for professional and subprofessional members of hospital staffs. To aid in these programs, the delegates recommended that the American Hospital Association, the American Medical Association, and the Public Health Service collaborate in producing and distributing training films and other educational materials. They also proposed that the Public Health Service produce and distribute widely to hospitals a manual containing all available information on environmental disinfection and on the sterilization of equipment, linen, and other objects used with patients.

9. Strengthening of laboratory services. By the phage typing process, it is possible to identify dangerous strains of staphylococcus and thus enable hospitals to trace the source of infection. However, since it is not practical for many institutions to do this, it was recommended that the Public Health Service, through its own facilities and by assisting state and local health department laboratories, should aid in performing phage studies, particularly in epidemic situations.

10. Expansion of research. Areas in which the delegates felt more knowledge was needed before recommendations could be made included (1) the effect of environmental contamination on the spread of infection; (2) desirable features in the design and construction of hospitals and hospital equipment, as the delegates believed that not enough is known about environmental factors in the spread of infection to warrant recommending extensive or expensive changes in existing structures; (3) the value of making staphylococcic infection a reportable disease. (Several states now require reports on all such cases and results in these states will be studied.)

The group also issued strong recommendations for basic research to determine why some people are more susceptible to infection than others and how a person's resistance to it can be strengthened, and also to find better methods of treating diseases caused by virulent and epidemic strains and ways of minimizing the development of drug-resistant strains.

Dr. Burney pledged the Public Health Service to do everything within its power to put these and other recommendations made by the conference into effect. The Public Health Service has already taken action on several of these measures. Applications for grants to carry on research on staphylococcic infections are being given priority consideration by the Advisory Councils of the National Institutes of Health and, through a special appropriation of one million dollars ear-marked for the study of staphylococcic infection, grants will be made this fall to support the most promising projects.

To assist states and communities in the rapid identification of epidemics, the Communicable Disease Center is preparing diagnostic reagents on a large scale. The Center has also assumed responsibility for operating the National Reference Center for Staphylococcal Phage Typing. Through its Epidemic Intelligence Service, the Center makes available specially trained physicians and nurses to help trace the source of epidemics and bring them under control. Training programs for laboratory and other personnel of state and local health departments have also been expanded by the Center.

Highlights of some other papers presented at the conference are as follows: Dr. R. Keith Cannan, chairman of the Division of Medical Sciences of the National Research Council, co-sponsor of the conference, explained that the council's interest in the problem stemmed from its study of the treatment of traumatic injuries, particularly burns.

Dr. R. E. O. Williams of the Public Health Laboratory Service, London, described the experience of the British, who were the first to isolate antibiotic-resistant strains of staphylococcus. He reported sample surveys in England which indicate that, apart from epidemics, about 5% of clean wound operations and 10 to 15% of newborn babies develop septic lesions. Describing the "wound books" which some English hospitals maintain on all operations, he said, "It is our feeling that systems which simply require notification of cases of infection are less likely to give complete records than those that demand recording of the outcome whether infection develops or not." He also advocated painting the umbilical stumps of newborn babies, a frequent site of infection, with antiseptic dye. Summarizing these and other English practices, he said, "There is no one way in which staphylococci spread in a hospital and there is no one prophylactic method by which spread can be prevented. The routes of infection are numerous and probably often devious and the precautions

needed are many and complex. . . . Our preventive measures have therefore to minimize the endemic level, to prevent the emergence of epidemics, and to terminate epidemics when they occur."

Dr. Robert J. Anderson, chief, Communicable Disease Center, Atlanta, cited the provision of adequate laboratory service, staffed by well-trained bacteriologists and technicians, within the hospital and at all levels of organized public health as a major need that must be met in order to apply the best available methods of controlling the disease. Noting that the indiscriminate use of antibiotics in medical treatment has been deplored by clinicians for years, he said, "The time is perhaps ripe for the positive approach—the formulation and promulgation of acceptable standards for the discriminate use of antibiotics."

Dr. Vernon Knight, associate professor of medicine, Vanderbilt University School of Medicine, Nashville, Tenn., described studies which indicated that, after patients have been in the hospital for a few days, the staphylococcic strains which they normally carry on their skins or in their noses are replaced by the drug-resistant strains which prevail in the hospital environment. After discharge from the hospital, the process reverses, with the normal strains replacing the drug-resistant strains.

Dr. Thomas E. Shaffer, professor of pediatrics and preventive medicine, Ohio State University College of Medicine, Columbus, speaking on outbreaks of infections in nurseries, noted that they began about 12 years ago in England, subsequently occurred in Canada, Australia, and the United States, and finally throughout the world and were characterized in their early stages chiefly by conjunctivitis and impetigo. "Failure to recognize these commonplace and seemingly unimportant lesions as forerunners of disastrous epidemics in which serious complications have occurred has allowed epidemics to progress before control measures were established," he said. One particular strain, 80/81, is responsible for the majority of these epidemics in all parts of the world.

Dr. Chester W. Howe, associate professor of surgery, Boston University School of Medicine, said, "In terms of morbidity, prolongation of hospital stay, economy, necessity for further surgical risk, and particularly from the point of view of massive contamination of the hospital environment . . . postoperative staphylococcal infections are a particularly important problem in surgery." Although the pathways by which staphylococci gain access to a clean wound are not known, he reported suggestive evidence which indicates that the majority of such infections begin in the operating room. He urged extensive study of the problem and said, "There is no doubt that its significance is of such extent that it warrants the expenditure of the large amount of money and effort which would be required."

Dr. David E. Rogers, associate professor of medicine, New York Hospital–Cornell Medical Center, New York City, stated, "In contrast to the experience of pediatric and surgical services, staphylococcal infections in non-operated adults on medical wards are nonepidemic, occur in a small number of patients, and have been relatively constant in incidence for a number of years."

Dr. Frederick H. Wentworth, medical director of disease control activities, Ohio Department of Health, Columbus, cited case histories indicating the seriousness of family infections resulting from patients carrying the disease home from the hospital. In one family, an infant was discharged from the hospital in October, 1954, and soon showed symptoms of a hospital-acquired impetigo. From then until July, 1958, there has never been a time when one or more of the five members of the family did not have some infection, and the cost of their care, exclusive of hospital bills, has been more than $1,500.

Dr. John E. Blair, bacteriologist, Hospital for Joint Diseases, New York City, pointed out that it is not practical for most hospitals to do their own phage typing of strains since it is hard to maintain the phages and requires highly trained personnel to do the typing. He advocated the use of regional laboratories as means of keeping better control over the quality of phages and of assuring the consistency of tests. He suggested that cultures be submitted only on a series of related sources, not on isolated cases.

Dr. John C. Colbeck, chief of service in the pathology department, Shaughnessy Veterans Hospital, Vancouver, British Columbia, Canada, suggested that small hospitals may afford especially good opportunities to study how infections spread. "In large hospitals, the possible routes of spread are so numerous that the probable method of spread is all too often indeterminable. . . . It might be wise for public authorities to consider the establishment of research units, with full laboratory facilities, in the smallest hospitals."

Dr. Dean A. Clark, general director, Massachusetts General Hospital, Boston, declared that hospital-acquired staphylococcic disease is always a community problem, never limited to the four walls of a particular hospital, since many, if not most, infections in patients become apparent only after discharge. He urged that hospital administrators plan to follow up at least a random sample of discharged patients and make suitable arrangements with their medical staffs, other hospitals in the area, and the health department to collaborate in such follow-up procedures in order to assure the detection of all related cases.

Leaders of the work groups who developed recommendations based on the data presented by the speakers were Dr. Warren E. Wheeler, professor of pediatrics, Ohio State University College of Medicine, Columbus; Dr. William A. Altemeier, professor of surgery, University of Cincinnati College of Medicine; and Dr. Ivan L. Bennett Jr., professor of pathology, Johns Hopkins Hospital, Baltimore.

Chairmen of the general sessions were Dr. Isidor S. Ravdin, professor of surgery, Hospital of the University of Pennsylvania, Philadelphia; Dr. Morris Tager, professor of bacteriology and immunology, Emory University, Atlanta; and Dr. Anderson.

Dr. Harry F. Dowling, professor of medicine, University of Illinois College of Medicine, Chicago, summarized the conference. Discussants of the papers were Dr. Mark H. Lepper, professor of preventive medicine, University of Illinois College of Medicine, Chicago; Dr. Reimert T. Ravenholt of the Seattle-King County Department of Public Health, Seattle; and Dr. H. Taylor Caswell, clinical professor of surgery, Temple University School of Medicine, Philadelphia.

THE LEISURE CORNER

SEARCHING FOR TREASURE

Collecting, once the avocation and passion of monarchs and royalty, has undergone a process of extensive democratization. Today millions of people everywhere find collecting a fruitful recreation. It is especially exciting if one falls heir, probably for the first time, to an accumulation of trash piled high in an attic, a barn, a store, or a shop. Of course your first reaction may be to dump the stuff, but before you throw away a single item consider the possibility that there may be a treasure of some kind in each pile of litter. There are gold mines to be found in attics and cellars and treasure troves in overlooked nooks and corners. Occasionally a cache of money is stuffed in an old sofa, under a loose board in the floor, or in the bottom of an old clock.

During periods of war and national stress some people hide coins and bills in the strangest places, in chimneys, table legs, framed pictures, and wells. Much of the stuff hoarded for no apparent reason —books, pamphlets, newspapers, catalogs—in out-of-the-way places may have some monetary value. A leading auction gallery in Washington, D. C., displays the following axiom: "The junk of one generation is the treasure of the next." Not long ago a physician in his 70's stood at a booth in an antique show holding a toy in his hand and muttering, "I just can't believe it. I just can't believe it." The toy was a small tin boat holding a little man with a pair of oars. A spring was wound and the little tin man rowed the boat on a small pond. The price tag read $65. What the elderly physician could not believe was the series of events that had transpired. Only about a month before he had thrown this particular toy and scores of similar items into a box which he literally paid a trashman to cart off. In the very town in which he resided an antique dealer purchased the "junk" from the trashman for a dollar. One object, the small mechanical toy rowboat, finally came to rest on the shelf of another antique dealer with a price tag 65 times the original price of the toy that had been manufactured many decades before.

Similar occurrences take place thousands of times a day in the United States. Daily the unbelievable happens when treasures are discovered in so-called trash. More often, however, accumulations of trash are burned or sold as scrap paper or scrap metal. One senses lost opportunities, picturing the treasures that go up in smoke, are melted down in furnaces, or are converted to pulp in paper mills. At the same time one can get the lift of a lifetime envisioning the possibilities of the search for treasure. Take the case of a woman who found a letter that just missed being consigned to the furnace. The letter was from the daughter of the owner of the early nineteenth-century house which she had purchased. The daughter had gone to the Sandwich Islands as the wife of a missionary. For more than 20 years she wrote a weekly letter to her parents, and when the Sandwich Islands, properly Hawaii, began using postage stamps the daughter unwittingly laid the foundation for a most valuable collection. In short, what gives value to the treasures that may be found in trash is a combination of the factors that people hold dear, from mere fashion to sentimental significance or rarity.

It is quite common to see book collectors avidly searching through secondhand book stores for volumes that are off the beaten track. Some of these persons are professional book dealers, others are hobbyists. Each book is valued not necessarily because some author has poured his soul into words, but for its market value. From this vantage point, searching for the unusual in books can be a profitable hobby. It is a hobby not to be sneezed at, unless, of course, allergic tendencies to paper and dust manifest themselves. The dedicated bibliophile cares deeply about what a book says and what the author's intent is. The bibliophile wants to help disseminate the message of the author. The conventional book collector, however, derives pleasure from seeing a book listed in a catalog at a price

two or three times what he had paid for it. If he is a dealer he will look for a customer, in the hope of making a sale at a profit. It is interesting to note that in the field of books there are more potential purchasers of rare and scarce items than there are items available. The possibility of finding a literary treasure in a home library, a trunk, or a box of old books is never extinct.

In the decades between 1910 and 1940 Americans spent more than a billion dollars for items gathered and collected under the guise of trash. One person who was responsible for the awareness of the value of discarded material, and who made a fortune reselling articles to the upper crust of American society, was Elsie de Wolfe. She made collecting a serious and profitable part of her life, searching, investigating, not missing a single article that potentially contained a hidden fortune. She once became fast friends with a retired physician whose hobby it was to collect pictures, photographs, and advertisements dealing with invalids' chairs and velocipedes. He used to look for those advertised in newspapers, buy them, and then improve their designs. When he was ready to sell the chairs and velocipedes, she would offer him a modest fee, then resell the articles to curators for extravagant sums of money. Once started, the fashion of collecting was off in a cloud of dust, and, to mix metaphors, it snowballed, multiplied, and became a tidal wave. Were Elsie de Wolfe alive today it is conceivable that she would be organizing a rocket trip to the moon to look for junk.

After one has learned the various techniques and methods of recognizing and sorting the classified treasures in an accumulated basket of trash, he should try out on an antique dealer an item that looks like a "sleeper." Occasionally his poker-faced countenance may give you an inkling that you have something of value.

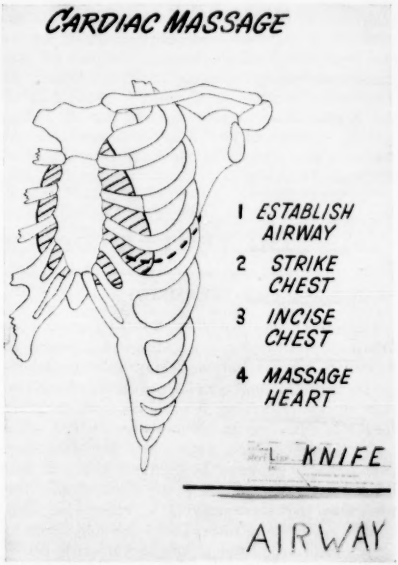
A number of years ago a physician became interested in collecting small patent medicine bottles, later adding flasks and other types of medicinal containers. His heirs, having no idea of the value of these bottles, disposed of them cheaply to a junk dealer when actually they were worth a modest fortune as medicohistorical items.

The thrill connected with searching through trash and junk is in no way diminished because some people regard it as downright silly. Think of the distinguished collectors of the past who have contributed to the present because they sensed the deeper meaning of the statement that the junk of one generation is the treasure of the next. Then go out and have some pleasure—and profit—in searching for that treasure.

CORRESPONDENCE

CARDIAC EMERGENCY

To the Editor:—Cardiac massage has become an accepted emergency procedure for use in indicated cases on the hospital floor and emergency room as well as in the surgery suite. Unfortunately the necessary equipment is not as readily available as in the operating room, and the time spent accumulating it can spell the difference between success and failure.



Poster showing directions for cardiac massage as emergency procedure.

Because of this, I have devised a simple and inexpensive poster that can be tacked in an unobtrusive location on each floor of the hospital (see figure). The 22-x-16 in. poster contains brief directions and a diagram of the chest wall illustrating the site of incision. In the lower right corner in sterilized syringe bags are a large surgical knife and a plastic airway.

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MEDICAL LITERATURE ABSTRACTS

INTERNAL MEDICINE

Shock and Acute Abdominal Symptoms Complicating Acute Idiopathic Pericarditis. H. R. Witherbee Jr. and M. L. Pearce. Ann. Int. Med. **49**:876-884 (Oct.) 1958 [Lancaster, Pa.].

The authors present the histories of 3 patients, which illustrate the occurrence of shock and of acute abdominal symptoms in association with acute idiopathic pericarditis. One of the patients in whom the presenting symptom was shock had an elevated serum glutamic oxalacetic transaminase activity. This was an unusual finding, and it probably reflected a severe degree of pericardial inflammation with concomitant subepicardial myocardial injury. Blood pressure rose promptly after the administration of arterenol to both patients with shock.

Abdominal pain may be a major symptom of acute pericarditis. When pain is initially confined to the abdomen and is accompanied by tenderness with guarding, the possibility of acute pericarditis can be easily overlooked, the more so since pericarditis occurs chiefly in subjects, between 20 and 40 years, in whom it may seem unnecessary to rule out cardiovascular disease before laparotomy is resorted to. Electrocardiography and frequent precordial auscultation may demonstrate the true etiology of what at first sight appears to be an "acute surgical abdomen."

Coronary Embolism: Review of the Literature and Presentation of 15 Cases. N. K. Wenger and S. Bauer. Am. J. Med. **25**:549-557 (Oct.) 1958 [New York].

In the years 1929-1957 there occurred at Mount Sinai Hospital in New York 11 well-documented cases of coronary artery embolism, which were confirmed by postmortem examination, representing an incidence of 0.06% in 17,469 consecutive autopsy cases. In addition, during the 6-month period from January through June, 1957, 3 unsuspected cases of coronary artery embolism, incidental to the cause of death, were found at postmortem examination. These 14 cases and 1 other recently brought to the attention of the authors are presented. The literature regarding this disorder is reviewed. Coronary artery embolization presents as an acute cardiovascular episode characterized by varied combinations of pain, shock, arrhythmia, and pulmonary edema. It must be a consideration in the differential diagnosis of sudden death in a young adult.

Two-thirds of the patients with bacterial endocarditis as the underlying disease died suddenly as a result of the coronary embolism; one-third of the patients in whom death was due to coronary embolism had a more protracted clinical course, presenting with an acute myocardial infarction. Among the patients with an etiology other than bacterial endocarditis, all the deaths from coronary embolism occurred suddenly. This sudden death may be related to the nature of the embolic material, to the underlying disease, to the general condition of the patient, or to the fact that in patients dying later in the course of their disease the diagnosis was incorrect, as they were considered to have had a coronary thrombosis without a search being made for emboli.

Coronary artery embolism is primarily a disease of the younger age group. Fifty of 71 patients were under 40 years of age, and all but 5 were under 60 years of age. The criteria for the diagnosis of coronary embolism as the cause of death included the presence of an occluding mass in a major branch of the coronary artery, identification of the site of origin of the embolus, and the demonstration of an essentially normal arterial intima at the area of occlusion.

Muscular Metastases as First Symptom of Cancer of Lung. T. G. Villar. Med. contemp. **76**:368-374 (Aug.) 1958 (In Portuguese) [Lisbon].

Muscular metastases as an early symptom of cancer of the lung are extremely rare. If they do appear, they are generally few and very small. A man, 50 years old, was admitted to the Hospital of the University of Lisbon with an illness of 3 months' duration, characterized by the appearance of diffuse, rapid growing nodules mainly located in the thorax and at the hips. The nodules were large and extremely painful, varying in size from that of a hen's egg to that of the head of a fetus. The patient had no appetite, could sleep but little, had

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lost 10 kg. (22 lb.) in weight, and complained of a chronic cough. He had had pneumonia on the left side twice in the last 3 years. Occasionally he expectorated blood. Repeated roentgen-ray examination of the chest showed bilateral shadows in the lungs, leftward deviation of the mediastinum, and rapidly progressive interstitial sclerosis of the lungs. The sputum was negative for tubercle bacilli. It was histologically positive for malignant cells. A tumor of the main bronchus was seen on bronchoscopy. Bronchoscopic biopsy showed adenocarcinoma. Histological study of a cervical node revealed metastases of adenocarcinoma. The nodules grew rapidly, acute respiratory symptoms appeared, and the patient died 2½ months after hospitalization. Autopsy showed primary bronchogenic carcinoma, with multiple metastases to the lungs, pericardium, viscera, lymph nodes, pleura, peritoneum, vertebrae, muscles, and bone marrow of the long bones. The author reviewed 850 autopsy records of the department of pathological anatomy of the university hospital for patients who died of cancer in the last 17 years. Pulmonary cancer was reported in 91 cases, and muscular metastases in 15 of these cases. The muscular metastases were few and small in all the cases but the one reported by the author. In 5 of the 15 autopsy records in which muscular metastases were reported, the primary cancer was a bronchogenic carcinoma.

Thromboembolic Pulmonary Diseases Illustrated by Clinical Examination and Autopsy Findings in Larger Hospital Material. N. Bang, K. Iversen and H. Schmidt. Nord. med. **60**:1413-1416 (Oct. 2) 1958 (In Danish) [Stockholm].

Attention is directed to the frequency of thromboembolic pulmonary diseases and the grave threat they present to surgical and medical patients in spite of early mobilization possibly supplemented by anticoagulant treatment. Thromboembolic pulmonary disease was established in 271 of 1,788 persons, aged over 15 years, on whom autopsies were performed at a Copenhagen hospital in 1954-1955. The occluding processes comprised thrombi, emboli, and infarctions. The frequency of thromboembolic pulmonary diseases increased as the age increased. In 84 cases the course was acute, with death within 24 hours after onset of the symptoms; in 33, subacute, with death within a week; and in 26, chronic, with duration of over a week. In 128 cases there was a larvate course, and the time of origin of the symptoms could not be established; the group consisted partly of cases with insidious development of a pulmonary thrombosis or embolism and slow progression of symptoms, partly of a larger number of cases in which other grave diseases so strongly stamped the clinical picture that the pulmonary embolism escaped notice. The diagnosis was made during life in only one-sixth of the cases. Diagnosis was overlooked particularly in old and weakened patients. In every case of suddenly originated tachycardia and of sudden aggravation of an existing heart insufficiency and on every rise in temperature in bed patients in poor condition, the possibility of a pulmonary embolism must be borne in mind. If antibiotic treatment is given on suspicion of bronchopneumonia, pulmonary embolism must be considered if the temperature does not fall and the condition does not improve. If there is insufficiency with rapidly increasing cyanosis and dyspnea and gradual development of electrocardiographic changes pointing to cor pulmonale, the possibility of thrombosis of the pulmonary artery should be considered.

Action of Streptomycin and of Isonicotinic Acid Hydrazide on Tuberculous Cavities. U. Massola. Minerva med. **49**:3471-3488 (Sept. 12) 1958 (In Italian) [Turin, Italy].

A combination of streptomycin and isonicotinic acid hydrazide was administered to 162 patients with tuberculous cavities for a period of 100 to more than 200 days. The daily dosage of streptomycin was 1 Gm., and that of isonicotinic acid hydrazide ranged from 250 to 300 mg. Cavities of recent date were present in 78 patients; recurring cavities, in 24; and chronic cavities, in 60. The combined therapeutic action of streptomycin and isonicotinic acid hydrazide brought about the best results in patients with tuberculous cavities of recent date which were small in diameter. Cavities were healed in 62 patients (38.2%), healing being obtained in 46 with cavities of recent date, in 12 with recurring cavities, and in 4 with chronic cavities. It seems that prolonged therapy, rather than the size of the daily dosage, was the decisive healing factor. The antibiotic treatment of tuberculous cavities must be supported by other common therapeutic measures.

Mediastinal Teratoma with Metastizing Chorioepithelioma. A. Hallén and S. Holmberg. Nord. med. **60**:1432-1433 (Oct. 2) 1958 (In Swedish) [Stockholm].

Teratoid tumors are relatively rare formations which usually originate from the genital glands. Other places of predilection include the anterior mediastinum. The tendency to malignity is high in the embryonal teratomas of various localizations. The most common degeneration is carcinoma; chorioepitheliomas can also occur. In the case reported in a youth, aged 19 years, with acute hemorrhagic pericarditis, there was moderate gynecomastia with secretion of colostrum. The chorionic gonadotropin titer was high. Roentgenologic examination of the chest revealed a tumor-suspect density in the left lung. The disease progressed rapidly, with fatal outcome in a month. At autopsy a large

mediastinal teratoma was found, with multiple metastases to the lungs, pericardium, kidneys, and liver. The testes were normal. If gynecomastia with secretion of colostrum is found in adult males, chorioepithelioma is highly probable. If the testes are normal, an extrangenital tumor should be looked for.

Hereditary Hyperparathyroidism Associated with Recurrent Pancreatitis. C. E. Jackson. Ann. Int. Med. 49:829-836 (Oct.) 1958 [Lancaster, Pa.].

Six and possibly 7 patients with hyperparathyroidism were observed in 2 generations of one family, and in at least 2 of these patients the hyperparathyroidism was associated with recurrent pancreatitis. The hyperparathyroidism was proved in 2 brothers and a maternal uncle and aunt by excision of parathyroid adenomas and was established in their mother and another uncle by repeated demonstration of chemical abnormalities. The pedigree of hyperparathyroidism in this family suggests an autosomal dominant type of inheritance, with both males and females affected in 2 generations. The pedigrees of hyperparathyroidism in families reported in the literature are also compatible with a dominant inheritance.

In speculating on the relationship between hyperparathyroidism and recurrent pancreatitis, the author says that the most attractive theory would seem to be that the pancreatitis is secondary to stone formation in the pancreatic duct system as a result of the hypercalcemia and alkaline pancreatic secretion. The relief of symptoms of recurrent pancreatitis by parathyroidectomy in the 2 brothers in this study and in the one case reported by other investigators also suggests that the pancreatitis was in some way sequentially related to the hyperparathyroidism. However, the possibility cannot be excluded that hereditary pancreatitis could be coexisting in this family. It is planned to perform urinary amino acid studies on affected and nonaffected individuals of this family, in accordance with the suggestion of Gross, Comfort, and Ulrich that this type of study will help to distinguish the hereditary from the nonhereditary form of pancreatitis.

Interpretation of Hematologic and Serologic Findings in the Diagnosis of Infectious Mononucleosis. C. E. Bender. Ann. Int. Med. 49:852-865 (Oct.) 1958 [Lancaster, Pa.].

In the author's observations on 600 patients with infectious mononucleosis, most of whom were seen in a university population, the differential counts were regularly characterized by a lymphocytosis. The diagnosis was further substantiated by high atypical lymphocyte counts and by heterophil antibody titers as well as by clinical manifestations. The lymphocytosis was not a transient finding but was present day after day during the acute phase and early convalescence. In the absence of straightforward clinical features, both the serologic and the hematological criteria should be fully satisfied before making the diagnosis of infectious mononucleosis. From the laboratory standpoint, the basic screening procedure is the identification of atypical lymphocytes. The nonspecific nature of these cells has contributed to a willingness to regard their presence as unessential. The author's own findings indicated that atypical lymphocytes are almost pathognomonic of infectious mononucleosis. Blood smears, as prepared in the average laboratory for routine differential counts, are unsatisfactory for the identification of atypical lymphocytes. Smears should be made about one-half the usual thickness, should be well stained, should have little overlapping of cells, and should be made during the febrile period of the disease. Later in the illness it will not be possible to differentiate atypical lymphocytes from other mononuclear cells with the same degree of certainty. Neutrophils are studied separately. Inspection of the records of 200 patients seen early in the illness by the author revealed that the lowest neutrophil count coincided in some patients with the peak of the fever; in most, however, the count was lowest about the time the temperature returned to normal. The relative value of neutrophil counts late in the illness is enhanced because of the uncertainties in identification of mononuclear cells at this stage of the disease. In the series studied the average neutrophil percentage was 22.2; the range was from 6 to 49%. All the patients tested had less than 50% neutrophils; 96% had less than 40% neutrophils.

In general, a differential absorption formula, showing little or no absorption of the antibody by guinea pig antigen and complete absorption by beef-cell antigen, is diagnostic of infectious mononucleosis. Minimal serologic evidence needed to make the diagnosis is as follows: with unabsorbed serum, a sheep-cell agglutination titer of 1:56; after absorption of the serum with guinea pig kidney, a titer of 1:28, at least 1:14. After absorption with beef-cell antigen, no agglutination of sheep cells should occur. Without a typical clinical syndrome, a differential absorption test of this low order of specificity should be rechecked. Readings are made macroscopically after 2 hours' incubation at room temperature. A practical point in the heterophil test is the question of reading after overnight refrigeration versus incubation at room temperature for 2 hours. The original Paul-Bunnell technique called for readings made after overnight refrigeration of the tubes. This practice has been abandoned, since it may result in falsely high titers.

While positive presumptive tests for heterophil antibodies have been reported in many disease states, no positive differential absorption test for infectious mononucleosis-type heterophil antibodies

can be duplicated by any other condition. The need for differential absorption tests should be based more on atypical clinical and hematological features of the illness than on titer levels alone. Heterophil antibodies persisting from earlier, unrecognized attacks of infectious mononucleosis may sometimes explain the paradox of a positive heterophil test unaccompanied by characteristic clinical and hematological features of this disease. There is also evidence that other diseases may cause a resurgence of heterophil antibodies. These considerations emphasize the fallacy of basing the diagnosis on a positive heterophil test per se. While either a mononucleosis or a positive heterophil test gives assurance that the disease is infectious mononucleosis, each may occur independently in other situations. Not one or the other but both are essential to the diagnosis of infectious mononucleosis.

Congenital Hemolytic Anemia with Abnormal Pigment Metabolism and Red Cell Inclusion Bodies: A New Clinical Syndrome. R. D. Lange and J. H. Akeroyd. Blood **13**:950-958 (Oct.) 1958 [New York].

The presence of abnormal inclusion bodies in erythrocytes after the ingestion of toxic substances is well known. The authors recently had the opportunity of studying a 14-year-old patient who was known to have had a hemolytic anemia since infancy. Routine hematological studies revealed unusual inclusion bodies in about 14% of her erythrocytes. There was no history of ingestion of toxic substances. The child passed a dark brown or blackish colored urine. Because it is felt that this probably represents a new clinical entity, the case history and results of special studies are reported. The diagnosis of a congenital hemolytic anemia was based on the following facts: 1. The anemia had been present since at least the age of 30 months. 2. Hemolytic disease had been demonstrated by transfusion studies which were also diagnostic of an intracorpuscular defect. 3. The Coombs tests had been consistently negative except when undiluted serum was used (this may be explained on the basis of the reticulocytes being Coombs positive). It is of interest that no abnormalities could be demonstrated in the erythrocytes of the parents.

The inclusion bodies remained unclassified in the patient studied. They did not resemble Pappenheimer bodies in that they were not rod-like, and they were not siderin. Howell-Jolly bodies were also present in this patient, but they were easily distinguishable from the inclusion bodies. The inclusion bodies resembled Heinz bodies in some of their morphologic and physical characteristics in that they were globular, refractile, and irregular in shape, stained with crystal violet, and were insoluble in water. However, they were visible when stained with Romanovsky dyes, whereas Heinz bodies are visible only by use of vital dyes or dark-field microscopy. The authors suggest that the syndrome be named "congenital hemolytic anemia with abnormal pigment metabolism and red cell inclusion bodies."

The Nephrotic Syndrome in Adults: A Common Disorder with Many Causes. R. M. Kark, C. L. Pirani, V. E. Pollak and others. Ann. Int. Med. **49**:751-774 (Oct.) 1958 [Lancaster, Pa.].

The metabolic, nutritional, and clinical consequences of continued massive albuminuria constitute the nephrotic syndrome. From the experience of the authors with 98 adult patients studied by renal biopsy, it is apparent that the syndrome may be due to a variety of causes and different pathological changes in the kidney. It may be the result of (*a*) primary renal disease, such as lipid nephrosis or glomerulonephritis, (*b*) renal disease associated with systemic illnesses, such as diabetes mellitus, systemic lupus erythematosus, or amyloidosis, or (*c*) pressure effects on the venous system draining the kidney, e. g., renal vein thrombosis or constrictive pericarditis. The authors tabulate the histological diagnoses in 98 patients, ill with the nephrotic syndrome, who were studied by biopsy.

Glomerulonephritis was diagnosed in 46 patients, of whom 28 had the membranous type, 12 had the mixed (membranous and proliferative) type, and 6 had the proliferative type. In 11 patients the histological signs were typical of lipid nephrosis, which the authors define as a condition of unknown etiology characterized clinically by the nephrotic syndrome and having a good prognosis. No definitive structural changes were observed in the glomeruli of these 11 patients with the nephrotic syndrome when renal biopsies were made during or immediately after the edematous phase. There was degeneration of the tubules, the lining epithelium of which contained fat, and there was edema of the interstitial tissue. No significant abnormality could be demonstrated in the glomeruli. Clinically these patients did well. All those treated with corticotropin (ACTH) or adrenal corticosteroids had an excellent diuresis. No patient developed permanent hypertension or evidence of renal failure.

Lupus nephritis (systemic lupus erythematosus) was the cause of the nephrotic syndrome in 18 of the 98 patients. The course of the renal disease was usually rapid, and death occurred within a few months to 3 years in most patients. Diabetes mellitus was the cause of the nephrotic syndrome in 15 patients, which syndrome could not be related to the type of treatment given. The nodular glomerular lesions described by Kimmelstiel and Wilson were found in 14 of the 15 diabetics with the nephrotic syndrome. Of the remaining 8 patients with this syndrome, 3 had renal amyloidosis and 1 had severe arterial and arteriolar nephrosclerosis. Of the 4 patients in whom the nephrotic syndrome

was associated with increased pressure in the renal veins, 2 had thrombosis of the renal vein, 1 had constrictive pericarditis, and 1 had tricuspid stenosis.

Treatment in the nephrotic syndrome should be directed toward the edema, to the underlying renal condition, and to specific etiological factors when these can be determined. At present treatment is largely of a nonspecific nature, although with increasing accuracy in diagnosis this will change. Salt restriction is designed to prevent edema and to initiate diuresis, and while low-salt diets are widely prescribed, little attention is paid by many clinicians to ensuring that these are sufficiently low in sodium. Limitation of salt intake is now relatively easy with low-sodium milk powders. In some patients with severe and prolonged proteinuria, deficiencies of both calcium and potassium may occur, with resulting bone rarefaction and hypokalemia. Both these defects are corrected by high-protein diets, with the use of low-sodium milk powder, although additional potassium may be required in the early stages of treatment. The value of steroid therapy in the nephrotic syndrome is still to be determined. Many have used ACTH or cortisone in short courses for from 10 to 15 days, with large doses simply as a "diuretic," and there is little doubt that many patients will show loss of weight and of edema with this treatment.

Fungus Disease in Northern California. L. A. Rantz, C. Halde, D. Newstrand and D. Kettner. California Med. **89**:245-249 (Oct.) 1958 [San Francisco].

In an attempt to get information concerning the importance of fungi as cause of disease in northern California, the authors studied specimens from superficial lesions, such as hair, skin, and fingernails, obtained from 1,544 patients. Potential pathogenic fungi, particularly Microsporum audouini, Trichophyton rubrum, and T. tonsurans, were found in 542 specimens. These findings indicated that superficial mycotic infections were commonplace but that systemic illness caused by these organisms was uncommon.

The authors report on 1,449 patients from whom sputum, bronchial and gastric washings, pleural fluid, collections of pus, and other clinical materials were obtained and studied for systemic fungous infections in the department of medicine of Stanford University. Three hundred sixty-one of these patients were infected by Coccidioides immitis, Nocardia asteroides, Actinomyces bovis, or Cryptococcus neoformans. Most of these examinations were made routinely without reference as to whether or not the patient was thought to have a mycotic disease. Infection by these 4 kinds of fungus was proved in 8 patients in the whole group in whom disease caused by these organisms was considered possible. The incidence would have been greater if the source of the materials had been more carefully screened. In several of the 8 patients the clinical situation suggested mycotic disease. It is evident that the routine examination of a large number of clinical specimens does not uncover many instances of unsuspected systemic fungous infection. Candida organisms in large numbers were recovered from the sputum, from material obtained on nasopharyngeal and vaginal swabs, and from stools of a considerable number of patients, many of whom had received antimicrobial therapy. It was nearly always difficult to assess the role of these fungi in the causation of various manifestations of the patient's illness. In no case was pulmonary candidiasis definitely diagnosed, and in only 3 cases was there positive evidence of disseminated infection caused by these organisms. Candida organisms of various species are often recovered from clinical materials, but the role they play in the causation of disease is always difficult to ascertain. Serious infection by this group of organisms is most likely to occur in debilitated persons who have received antimicrobial therapy.

Lymphogranuloma Venereum: A Review of 61 Cases. D. Erskine. Brit. J. Ven. Dis. **34**:163-165 (Sept.) 1958 [London].

This report is concerned with 61 male patients who were treated for lymphogranuloma venereum in the Seamen's Hospitals, London, between 1950 and 1957. With a few exceptions, they were admitted to hospital for treatment. Most of them presented in the venereal diseases department with a swelling in the groin; only a few were referred from the casualty department or from the surgeons, and consequently the author did not see the divers manifestations of this condition. In only 4 patients were transitory primary lesions detected. With one exception, all the patients were probably infected overseas, although not all gave a history of risk of infection, and they would often have passed the initial phase before presenting with a bubo. In some cases language difficulty, and in others the patient's lack of observation, may account for the absence of reported initial lesions.

The author suspects that some patients, in whom genital herpes, balanitis, and nonspecific urethritis were diagnosed at his clinic, may have later presented themselves with buboes at other clinics. He recalls one patient who reported with 3 tiny erosive ulcers in the coronal sulcus; there was no glandular enlargement, and a diagnosis of genital herpes was made, because routine investigations such as the Frei test were negative. The serologic complement-fixation test was reported positive to dilution 1:96 after the patient had left the clinic cured of his herpes a few days later. He returned 3 months later with a recurrence of the genital herpes, and now the inguinal nodes on the left were enlarged.

The Frei test was strongly positive, and the lymphogranuloma complement-fixation test was positive to dilution 1:144. It seems that a positive Frei test may be slower in developing than the serologic reaction, and one doubtful or negative test should not be considered final in the early stages of suspicious lesions. The incubation period of the bubo averaged 5 weeks.

Thirty-two of the 61 patients were treated with Terramycin, which the author considers to be the drug of choice—21 with two 10-day courses, separated by a 7-day interval (total 4 Gm.), and 11 with one course (20 Gm.). Nine patients were treated with sulfonamides alone, 6 with sulfonamides and Aureomycin, 7 with Aureomycin alone, and 7 with 3 courses of various combinations of sulfonamides and tetracyclines. The clinical response was satisfactory in 51 of the 61 cases. The significance of this clinical cure in relation to absolute cure is difficult to assess. The reversal of the serologic reaction was delayed, although, when it was possible to check the complement-fixation test a year or so later, reversal was found in the majority of patients in whom 2 or more courses of treatment had been given.

Anuria Complicating the Treatment of Leukemia. R. A. Kritzler. Am. J. Med. **25**:532-538 (Oct.) 1958 [New York].

Urinary suppression due to precipitation of urate in the urinary outflow tract occurs in leukemia more frequently, particularly after vigorous chemotherapy, than is generally appreciated, and presents a hazard that should not be ignored. The author reviews previously reported data on this problem and presents 3 new cases of which 1 was a case of acute leukemia. The first of the 3 new cases concerned a 65-year-old woman, in whom anuria and uremia were due to blockage of the ureters and renal pelves by urates excreted in increased amounts, presumably as a consequence of treatment with radioactive phosphorus. Fluid intake at the time of treatment was not sufficient. A diuresis followed pyelostomy. The precise cause of death was not clear.

The second case concerned a 63-year-old man, in whom anuria and moderately severe uremia occurred during the 10th week of a gradual fall in leukocytes while chlorambucil was given. Diuresis and recovery followed ureteronephrostomy and removal of urate precipitate on one side. Leukemic or nonleukemic renal failure seems excluded by the fact that prior to the anuria the patient received a course of triethylene melamine without renal complications, and later, when a course of chlorambucil was repeated with adequate fluid intake, there was no oliguria, crystalluria, or significant rise in the blood urea nitrogen level. The anuria is considered to have been a complication of therapy, probably precipitated by dehydration due to hot weather.

The third patient was a 41-year-old woman, in whom a number of factors contributed to the development of acute anuria. At the time treatment was begun there had been high fever and vomiting. The pretreatment serum nonprotein nitrogen elevation was probably due in part to dehydration and in part to renal insufficiency associated with leukemic infiltration of the kidney. The recorded fluid intake during the first days of cortisone treatment appeared inadequate. The fall of circulatory leukocytes from a high level was extraordinarily precipitous. The blood uric acid level reached 35 mg. per 100 cc.

Data on the 3 cases described and on the 7 previously reported are tabulated. All but 2 of the patients were over 50 years of age. Nine of the 10 patients had chronic leukemia (6 myeloid, 3 lymphatic). In all instances the number of circulating leukocytes was high before treatment was begun and was considerably lower at the onset of anuria. The interval from the beginning of treatment to the development of oliguria was short (2 or 3 days) in some cases and long (62 days) in others. The mortality from this complication was high; only 2 patients survived.

The author feels that the following factors are contributory to the development of this rare complication: (1) age, the 5th and 6th decades; (2) high urinary output of urate and tendency to calculus formation in the untreated patient with leukemia; (3) further increase in urinary urate excretion due to destruction of large numbers of leukocytes or to inhibition of the formation of leukocytes and associated incorporation of purines by the therapeutic agent; and (4) dehydration and inadequate volume of urine. It is advisable to recommend a high fluid intake to all patients with leukemia during the first few weeks of any kind of therapy directed toward reduction of the mass of leukemic cells.

Frequency and Classification of Glucosuria in Older Hospital Patients without Marked Symptoms of Diabetes: Frequency of Diabetes in Medical Department. J. Pedersen and N. I. Nissen. Ugesk. læger **120**:1319-1323 (Oct. 2) 1958 (In Danish) [Copenhagen].

In 10% of 260 afebrile patients, aged over 50 years, without recognized diabetes or glucosuria, whose first nocturnal specimen of urine did not give positive reaction with Fehling's solution, routine examination of an average of 4 24-hour specimens of urine with Tes-Tape in the course of the first 2 weeks of hospitalization revealed spontaneous glucosuria twice as often in men as in women. The amount of glucose determined quantatively by the ferric cyanide method was minimal and intermit-

tent. None of the patients showed glucosuria in all specimens, and half of them had glucosuria in only 1 out of 4 24-hour specimens. About 3% of all the patients had diabetes, about 3% were observed for diabetes, and about 4% had nondiabetic glucosuria. Comparison of the last-named group with a nondiabetic aglucosuria control group showed identical average fasting and 24-hour blood sugar levels and glucose tolerance curves, which is regarded as proof that this glucosuria group is nondiabetic. Comparison of the group of diabetic patients with intermittent glucosuria with an equal-numbered group of patients with diabetes without glucosuria showed higher fasting blood sugar and broader glucose tolerance curves and, on the average, higher clinical renal threshold in the second group. Partial diabetes in older patients is hard to diagnose, largely because the glucosuria is intermittent. The glucose-oxidase method does not exclude diabetes in spite of repeated negative reactions. The method must be combined with examinations of the blood sugar in suspected diabetic patients whose urine gives negative Tes-Tape reaction.

SURGERY

Carcinoma of the Head of the Pancreas: A Study of 21 Cases. R. B. Eaton. Canad. J. Surg. **2**:15-21 (Oct.) 1958 [Toronto].

Eaton shows that a renewed interest has developed in the treatment of carcinoma of the head of the pancreas and ampulla of Vater, since Whipple and associates in 1935 demonstrated the feasibility of pancreatoduodenectomy. Reviewing several series of cases reported in the literature, he finds that, although the operative mortality rate has been reasonable, survival in carcinoma of the head of the pancreas has been of short duration. On the other hand, lesions limited to, or originating from, the ampulla of Vater or duodenal mucosa present a brighter picture, and quite a number of 5-year cures have been reported. It seems that there is an unwarranted delay in the diagnosis and management of many of these cases before surgery is contemplated. Twenty-one patients with carcinoma of the pancreas were observed by the author in his own private practice during the last 6 years; 8 patients were found suitable for pancreatoduodenectomy, 8 had palliative operations, and 5 were considered beyond operative relief.

Pain was usually the first complaint, and it gradually increased in intensity. It varied in type from a mild colicky or spasmodic pain to a boring sensation; it was usually located in the mid-epigastrium or the hypochondriac region on the right. Occasionally, it was aggravated by the taking of food. Jaundice was the presenting symptom or sign in all but one patient, although in most patients it was not the initial symptom. Associated with these 2 main symptoms were anorexia, nausea and vomiting, fatigue, constipation, and loss of weight. The liver was enlarged in most patients. A tumor was palpable only in a few advanced cases. Preoperative therapy consisted of the administration of vitamins K, B, and C and glucose solutions and blood transfusions.

In 3 of the 8 patients subjected to pancreatoduodenectomy, an end-to-end (Billroth I type) gastrojejunostomy was carried out, the pancreatic stump being implanted end-to-side into the jejunum just beyond this anastomosis. The common bile duct likewise was implanted into the jejunum some distance beyond the latter anastomosis, and a side-to-side enteroenterostomy was made opposite the site of implantation of the pancreas. In the other 5 patients the open end of the jejunum was closed, and the common bile duct, the pancreatic stump, and the stomach were implanted (in that order from above downwards) end-to-side into the jejunum. The second method was found to be preferable, chiefly because it appeared to fit into the reconstruction more easily and reduced operation time by eliminating the enteroanastomosis. There were few digestive complaints after either method. One patient died as a result of the operation. Of the 7 patients who survived pancreatoduodenectomy, all remained alive and well for more than a year, 1 patient being still alive 30 months after operation and enjoying good health. The average survival in the 8 patients undergoing the palliative procedure was less than 6 months. Pancreatoduodenectomy is a justifiable procedure in many patients with carcinoma of the head of the pancreas.

Closed Surgery in Atrial Septal Defect: Report on 70 Cases. H. G. Davidsen. Acta chir. scandinav. **115**:343-361 (No. 5) 1958 (In English) [Stockholm].

The author reports on 26 male and 48 female patients, between the ages of 4 and 47 years, with atrial septal defects who were admitted to the department of surgery of Rigshospitalet in Copenhagen. The functional capacity of the patients was recorded preoperatively and postoperatively, and the patients were grouped in 4 functional classes according to the criteria laid down by the New York Heart Association in 1953. Two of the 74 patients died on the operating table before the correction of the defect. Surgical intervention was limited to an explorative atriotomy in 5 patients. Closed operative techniques were employed in the remaining 67 patients; the semicircular suture method was used in 15 of the patients, the circumclusion suture technique was used in 40, and atrioseptopexy was performed on 12. Six anatomic types of atrial septal defect were observed at the surgical intervention: (1) superior marginal defect; (2) central defect; (3) multifenestrated membranous in-

teratrial septum; (4) simple primum defect; (5) primum intermedium defect; and (6) persistent ostium atrioventriculare commune.

The results of the operative treatment were determined by measurement of the intracardiac shunts and by the changes in the cardiac murmurs and the heart volume. It was found that, if the murmurs had disappeared completely, or if the volume of the heart had been reduced to less than 75% of the preoperative volume, the shunt had been eliminated. The semicircular suture technique failed because the sutures pulled through the myocardial fibers; this technique was abandoned on account of the unsatisfactory results. Atrioseptopexy proved particularly valuable in patients with a superior marginal defect in whom both the defect and the accompanying anomalous drainage of the right pulmonary veins may easily be corrected. Circumclusion suture gave good results in patients with central defects and multifenestrated membranous septum, and fair results in those with simple primum defect. Difficulties, however, were met even in patients with central defects if these were located too close to the opening of the inferior vena cava. None of the techniques used were effective in patients with primum intermedium defect and with persistent ostium atrioventriculare commune. Open methods which make possible repair under direct vision are regarded as the only chance for surgical treatment in these cases, although even these methods may often fail because of the frequent presence of severe valvular malformations in patients with these types of defect.

The most important operative complications associated with the closed surgical methods are those interfering with the valvular function or the drainage of the pulmonary veins. An abnormally large valve of the inferior vena cava (valvula eustachi) may be the cause of impaired drainage of the inferior vena cava. A persistent septum spurium may conceal the anatomic conditions in patients with a superior marginal defect. The circumclusion suture may cause thrombosis if a part of the suture material is left uncovered by the septal endothelium, and in 5 of 7 cases this condition did not cause any untoward reactions. Anomalies of the cardiac rhythm were uncommon except in patients operated on with the aid of hypothermia. Some postoperative complications could probably be considered as specific for the operative techniques. Nodal rhythm or atrioventricular block occurred in some patients after circumclusion suture, but disappeared again later. Transitory paresis of the right phrenic nerve was observed not infrequently until a new operative practice was introduced by which the pericardium was opened at a good distance anterior to the phrenic nerve. The operative techniques employed did not differ significantly with regard to complications and mortality rate. In addition to the 2 patients who died on the operative table before the correction of the defect, 5 died postoperatively, including 1 who died 10 months after the operation. Six of the 7 deaths occurred in patients with pulmonary artery hypertension and 5 in patients in the functional classes 3 and 4. None of the patients having normal pressures and being grouped in functional class 1 or 2 died.

Hypophysectomy in Disseminated Cancer of the Breast. E. Andersson. Acta endocrinol. **29**:295-301 (Oct.) 1958 (In English) [Copenhagen].

Hypophysectomy was performed at the neurosurgical department of the University Hospital in Copenhagen on 50 women, between the ages of 39 and 72 years, with advanced cancer of the breast of from 1 to 6 years' duration, with diffuse metastases to bones and soft tissues, in whom all other methods of treatment such as irradiation and hormone therapy had failed. Immediately before the hypophysectomy the patients were given 200 mg. of cortisone by intramuscular route. In the operating room the patients were given 100 mg. of hydrocortisone dissolved in 500 cc. of dextrose solution as an intravenous drip. Immediately after the operation the patient received another intramuscular injection of 200 mg. of cortisone, and cortisone was given twice daily for the first 5 postoperative days in doses of 150, 100, 75, 50, and 25 mg. respectively. Maintenance treatment consisted of 25 mg. of cortisone given twice daily, and 100 units of thyroid extract were administered daily. The postoperative course on this regimen was smooth in most patients. There was a postoperative increase in the urinary output which resulted from the removal of the posterior lobe of the hypophysis in addition to that of the anterior lobe.

Hypophysectomy was tolerated well; only 3 patients died within the first 2 weeks. It produced a remission in 21 of the 50 patients operated on, with relief of pain and restoration of the temperature and blood to normal. Metastases remained stationary in 16 of the 21 patients, and regressed in 5. The average duration of the remission was about 8 months. The most favorable effects of hypophysectomy were obtained in menopausal patients. Patients with metastases to the liver and brain did not respond. Blindness in the right eye occurred in 6 patients in whom the optic nerve had to be cut because of technical difficulties in the course of the operation. Seventeen patients stated that they had lost the sense of smell after the operation. The reported data show that hypophysectomy can produce a remission of varying duration in otherwise hopeless cases of breast cancer with widespread metastases. There may be subjective improvement, relief of pain, and a considerably decreased consumption of analgesics in

some of the patients without remission. Hypophysectomy marks an advance in the treatment of patients with far-advanced breast cancer.

Arterial Catheterization Used for Pressure Measurement from the Left Ventricle in Patients with Chronic Constrictive Pericarditis. A. Actis Dato and F. Morino. Minerva med. 49:3296-3306 (Sept. 1) 1958 (In Italian) [Turin, Italy].

Intraventricular hemodynamic pressure in the left ventricle was measured by catheterizing the humeral artery in 10 patients with chronic constrictive pericarditis. Intraventricular hemodynamic pressure in the right heart was also recorded in 8 of these patients. The clinical findings showed that pericardial constriction, affecting in an equal degree the right and the left heart, was present in 3 patients, that a more severe constriction of the left than of the right heart was present in 5, that right ventricular insufficiency existed in 1, and that a mild form of pericardial constriction was present in 1. These findings were confirmed by intraventricular hemodynamic pressures measured by the cardiac catheterization technique. Ventricular fibrillation developed in 2 patients during the catheterization procedure. After a short pause, catheterization was resumed and completed without further disturbance.

This investigation justified the following conclusions: Cardiac catheterization is a useful means of examining congestion of either the right or the left ventricle. It can reveal on which side of the heart the pericardial constriction is more severe, and it can show that there is a correlation between the intraventricular hemodynamic pressure tracings from both ventricles and the clinical picture. Consequently, the intraventricular hemodynamic pressure tracings from both ventricles can be used as a guide to determine which side of the heart should be more exposed to surgical therapy. The authors suggest that arterial catheterization used for pressure measurement of the left ventricle should not be routinely used in patients with chronic constrictive pericarditis. It can be used only after the clinical examination, roentgenologic and angiocardiographic findings, and catheterization of the right heart have failed to formulate a clear picture of constrictive pericarditis, this being a necessary condition for instituting an effective surgical therapy.

Protrusion of Lumbar Disks Causing Marked Bilateral Weakness of the Legs. H. E. Storino, R. E. Siekert and C. S. MacCarty. Minnesota Med. 41: 687-690 (Oct.) 1958 [St. Paul].

Protruded or extruded lumbar intervertebral disks may so compress the cauda equina that the patient is rendered paraplegic with sphincteric disturbances and saddle anesthesia. A review of the records of 4,330 patients, who had undergone laminectomy at the Mayo Clinic for protrusion of a lumbar disk during the past 5 years, revealed 21 patients who had reduction in motor power in their lower extremities of 50% or more. These form the basis of this report. Less than 0.5% of patients operated on for protruded lumbar disks in the period under consideration had marked weakness of the lower limbs. Patients with slight weakness in one or both lower limbs were frequently encountered but were not included in this study. In the majority (19 patients) the onset of the episode which led to operation was well delineated, with the first symptom being sudden pain in the lower part of the back with or without concomitant pain in the lower limbs. The pain varied from mild to severe. After several days or a few weeks almost all these patients had unilateral or bilateral sciatica.

Although in a few patients the weakness developed within hours, in most the onset of muscular weakness was gradual over a period of 1 or 2 weeks. Furthermore, something usually seemed to precipitate or aggravate the weakness. Such acts as expelling an enema, sneezing in the bent-over position, gagging while brushing the teeth, or trauma in the form of strenuous muscular effort, such as lifting a heavy object, manipulative therapy, and leg traction, initiated the attack or converted a relatively mild one into one with marked muscular weakness. No correlation was found between the level of the disk involved and the distribution of pain. The pain, however, tended to decrease as the weakness appeared and increased. Sensory disturbances were noted in 18 patients and difficulty with the urinary bladder in 11; 10 of these 11 also had difficulty with the anal sphincter. Return of function after operation was excellent in 5 patients and good to fair in 7 of the 15 for whom adequate follow-up was available. In 3 patients no return of function occurred. Early diagnosis and operation are important in obtaining a successful result.

Homeoplastic and Alloplastic Transplantations of Aorta. K. Kremer and H. W. Heupel. Chirurg 29:448-453 (Oct.) 1958 (In German) [Berlin].

Eight male and 5 female patients, between the ages of 11 and 38 years, were operated on at the surgical clinic in Düsseldorf, Germany, for aneurysm of the thoracic aorta, extensive stenosis of the aortic isthmus, and severe degenerative changes in the wall associated with stenosis of the isthmus. A homeoplastic graft, 4 to 8 cm. in length, was used in 8 patients, and a cylindrical Ivalon sponge transplant, 4.5 to 7 cm. in length, was employed in 5. One of the 8 patients with free transplantation of homeoplastic aortic graft died of obstructive thrombosis which originated from an aneurysmatically

dilated intercostal artery located distal to the graft. The 5 patients in whom Ivalon sponge grafts were used were followed for periods up to one year, and the clinical results were highly satisfactory. Healing over of the grafts occurred without complications, such as effusion or allergy. The material seems to exert a specific plastic effect which leads to a rapid and close union within the suture area. The Ivalon sponge grafts have many advantages over the homeoplastic grafts: they are more easily available; they can be manufactured in any number, size, and form; they can be sterilized simply and safely and can be stored without any special care. No degenerative changes in the sense of atheromatosis or calcification have to be reckoned with when Ivalon sponge grafts are used. By the recent use of contrast-providing threads it has become possible to show the wall of the graft in the roentgenogram and hence to follow the outline of the graft in the roentgenogram and to prevent occasional complications by aneurysmatic dilatations. Careful control for additional years will, however, be required to obtain definite proof of the superiority of the Ivalon sponge grafts over the homeoplastic grafts.

Hazards Attending the Use of Esophageal Tamponade. H. O. Conn. New England J. Med. **259:** 701-707 (Oct. 9) 1958 [Boston].

Experience with the Sengstaken-Blakemore tube at the Grace-New Haven (Conn.) Community Hospital suggested that complications during the use of esophageal tamponade are more frequent, more varied, and more serious than generally recognized. The Sengstaken-Blakemore tube was employed on 81 occasions in 50 patients with esophageal varices who were hospitalized from 1950 to 1957 at this hospital. The nasogastric tube was usually passed according to the directions supplied by the manufacturer. The gastric balloon was ordinarily inflated with 100 to 250 ml. of air; the pressure maintained in the esophageal balloon ranged from 20 to 40 mm. Hg. The average period of intubation was 78 hours, ranging from 10 minutes to 12 days. The total duration of intubation per patient was 121 hours, ranging from 30 minutes to 30 days. In 19 of these patients major complications developed during esophageal tamponade; 9 of them died as a direct consequence of these complications. In 6 additional patients factors complicating esophageal tamponade contributed directly to the fatal outcome; rupture of the esophagus occurred in 1 of these. Potentially fatal abnormalities in the use of esophageal tamponade occurred during 55 of the 81 episodes. Obstruction of the airway, which was caused either by regurgitation and bronchial aspiration of bloody gastric secretion or by the displaced esophageal balloon, was the most serious complication. In addition to major complications, such as 2 deep erosions in the proximal portion of the esophagus just below the arytenoid cartilage, there were minor complications which led directly or indirectly to a fatal result. Only 10 patients were entirely free of these difficulties during esophageal tamponade. Forty-one of the 50 patients died.

Considering these fatal complications, the question arises: Should this form of therapy be abandoned? Despite these disturbing statistics, esophageal tamponade still plays an important part in the treatment of patients with bleeding esophageal varices, especially those unable to tolerate surgical intervention. Bleeding seemed to be controlled, at least transiently, by this treatment in approximately 70% of the patients. In view of the high mortality among patients with hemorrhages of esophageal varices, regardless of the type of therapy employed, it is reasonable to assume that many patients of this series who died of complications of esophageal tamponade would have died of other causes.

To prevent the most serious hazards of this therapy, more emphasis should be placed on a better understanding of the apparatus and on more careful observation of the patient. A new tube should be used for each treatment, and the gastric contents aspirated immediatly after intubation. Constant, or frequent, intermittent gastric suction should be performed to empty the stomach and to evaluate control of the bleeding. Nothing should be administered orally. When esophageal tamponade is being used, one error of technique or judgment or a single unlucky accident may be enough to set in motion a series of events leading to death. It behooves those who employ this apparatus to know it intimately, to use it carefully, to avoid predictable pitfalls, and to anticipate unpredictable complications.

Pulmonary Resections for Metastatic Lesions. J. L. Ehrenhaft, M. S. Lawrence and D. M. Sensenig. A. M. A. Arch. Surg. **77:**606-612 (Oct.) 1958 [Chicago].

The results of surgical treatment of proved metastatic pulmonary malignancy at the University Hospitals, State University of Iowa, Iowa City, are given. Fifty-five carefully selected patients underwent exploratory thoracotomy. Pulmonary resections were carried out in 37 of these patients. In the group of 28 patients who had resections for carcinoma, 3 are alive from 2 to 7 years postoperatively. Of 15 patients undergoing exploration but without resection, 3 are alive from 1 to 2 years after the operation. In the group of 9 patients who had resections for sarcoma, 1 patient is alive 5 years and 2 patients are alive 2 years after the operation. The 3 patients with metastatic sarcoma who had exploration but not resection died within 4 months. The number of patients involved is small, but the figures do not give the impression that the results

are better among the patients with metastatic sarcoma than among those with metastatic carcinoma, as found in data from another study. No indication that salvage of the patient is related to the type of pulmonary resection was found. In this series there is no correlation of the length of time between treatment of the primary lesion and the appearance of pulmonary metastatic disease with salvage of the patient. A long interval is not necessarily associated with an increased survival rate. The type of tumor and its biological behavior are probably the most important factors. The results of surgical treatment of metastatic pulmonary breast cancer have been so discouraging that it appears that pulmonary resection is not justified. Yet when distressing pulmonary symptoms can be relieved, operation seems justified, even though prolonged survival after removal of pulmonary metastatic neoplasms may not be obtained. This complex problem needs periodic reporting of results. Pulmonary resection for metastatic lesions is indicated in carefully selected patients, as a small percentage of them will be cured of their disease and others will receive palliation of distressing symptoms.

OPHTHALMOLOGY

Glaucoma Following Radiotherapy. R. F. Jones. Brit. J. Ophth. **42**:636-638 (Oct.) 1958 [London].

The author reviews previously reported cases of glaucoma after radiotherapy and presents another case. The patient was a 40-year-old woman, who complained of nasal obstruction on the right side. A large polyp was removed, which proved to be a mucoid adenocarcinoma. Between December, 1954, and January, 1955, the area was treated by radiotherapy. Later a right-sided Caldwell-Luc operation with removal of the right middle turbinate bone was undertaken, and, as a recurrence of the carcinoma was found in the middle turbinate, a partial posterior fenestration of the right side of the palate was performed with intercavity irradiation by radium.

The patient noted that the right eye was dry and the vision blurred in April, 1956, and sought an opinion on May 7, after 3 weeks of visual disturbance. The ocular tension (Schiötz) was 32 mm. Hg in the right eye and 27 mm. Hg in the left. Gonioscopy showed the angles to be of medium width. In the right eye newly formed tortuous blood vessels occupied the angle and overlaid the peripheral iris. On June 11, the ocular tension had reached 45 mm. Hg. A week later the visual acuity had deteriorated, and corneal edema was present. The ocular tension was then 50 mm. Hg, and the fundus remained hidden after that date. The patient was now in pain, and cyclodiathermy was performed on June 21. After this, ciliary injection, corneal edema, and an anterior chamber flare developed, and the ocular tension remained between 42 and 45 mm. Hg (Schiötz), although pilocarpine and Diamox were administered. Later cyclodiathermy was repeated, the patient became free of pain, and the tension fell to 22 mm. Hg. The visual acuity was now the ability to count fingers.

Theoretically, the radiotherapy could have disturbed the inflow-outflow balance by producing an occlusion in the anterior ciliary veins, in the vortex veins, or in the central retinal vein. However, the finding of dilated, tortuous, varicose, newly formed vessels in the iris and angle after radiotherapy may be considered the causative factor in the onset of glaucoma.

THERAPEUTICS

Acute Meprobamate Poisoning. L. W. Powell Jr., G. T. Mann and S. Kaye. New England J. Med. **259**:716-718 (Oct. 9) 1958 [Boston].

A review of the literature revealed 11 cases of attempted suicide with large quantities of meprobamate. The patients took amounts ranging from 10 to 40 Gm. of this drug, and all recovered. The symptoms varied from sleepiness through stupor and coma to complete respiratory and circulatory collapse. Coma, areflexia, and lowered blood pressure occurred in most patients. The pulse became rapid in most, but was slowed to 40 per minute in one. One patient was cyanotic, and another had slightly cyanotic lips. Four patients had pinpoint pupils, and 2 had dilated, fixed pupils. Treatment was in accordance with the symptoms. Gastric lavage occasionally recovered a considerable part of the ingested drug, and an oral airway was inserted in several patients to insure unobstructed respiration. Tracheal aspiration relieved respiratory embarrassment in one patient. A variety of central nervous system stimulants were used, such as dextro amphetamine sulfate, amphetamine sulfate, caffeine and sodium benzoate, pentylenetetrazol, picrotoxin, and coffee. The prognosis was generally good regardless of which analeptics were used. Meprobamate poisoning is often associated with hypotension which has been treated with intravenous infusions and vasopressor substances, such as phenylephrine and levarterenol bitartrate. Overhydration, however, should be avoided in these patients because of their flaccid state.

The autopsy findings for 2 women who succeeded in committing suicide by taking 12 and 20 Gm. of meprobamate are interesting, because they are apparently the first cases of death resulting from this tranquilizing drug. One woman weighed 110 lb. (50 kg.), and the other weighed 125 lb. (57 kg.). In the first woman 12 Gm. of meprobamate would represent a dose of 240 mg. per kilogram of body weight, and in the second woman 20 Gm. would represent 350 mg. per kilogram of body weight, both of which are below the lethal dose in animals.

The fact that other persons have survived the ingestion of much larger amounts of meprobamate suggests that early symptomatic treatment may sometimes be lifesaving in certain cases, although there may be individual variation in susceptibility to the acute toxic effects of the drug.

A New Depot Penicillin: Bipenicillinate of Diphenylpiperazine. H. Beerens and V. Macquet. Presse méd. **66**:1418-1419 (Sept. 17) 1958 (In French) [Paris].

Bipenicillinate of diphenylpiperazine (BPDP) (2,5-diphenylpiperazine bis-benzylpenicillin G) is a new penicillin salt composed of 2 molecules of penicillin G joined by a diphenylpiperazine link—a comparatively simple link free from toxicity. The new product is slow to dissolve in water or serum, and this probably explains its prolonged action. It has an antibiotic activity of 1,310 units per milligram. Experiments showing that the drug was well tolerated and that it produced high concentrations in the blood were soon followed by clinical trials in which equally good results were reported. The findings so obtained have been confirmed by the present study in which the authors investigated the levels of penicillemia found in patients after the intramuscular administration of BPDP, procaine penicillin, and Bipenicillin (a mixture of 600,000 units of procaine penicillin and 400,000 units of penicillin G).

Comparison of the 3 sets of figures obtained showed that, while the blood levels produced by each of these forms of penicillin were identical 3 hours after administration, the subsequent rate of decline was lowest for BPDP, so that 9 hours after administration the levels produced by this drug were higher than those produced by the other 2. The injection of one million units of BPDP produced blood levels of more than 1 unit per milliliter in 15 minutes, and a maximum concentration of more than 3 units per milliliter in one hour. The prolonged action of the new penicillin was shown by the fact that effective therapeutic concentrations were still present 12 and 24 hours after injection. Tolerance for BPDP was perfect; the intramuscular injections were painless, and none of the patients suffered any cutaneous or anaphylactic reactions.

A Clinical and Laboratory Comparison of the Effects of Commonly Used Vasodilator Drugs on Arterial Diseases. J. M. Stallworth, W. H. Lee, C. Belisle and D. B. Nunn. Am. Surgeon **24**:700-708 (Oct.) 1958 [Baltimore].

Arlidin, Ilidar, Priscoline, and Drug 5029 were used in this investigation. Nylidrin (Arlidin) hydrochloride is a synthetic compound belonging to the epinephrine–ephedrine group. Its primary sympathomimetic actions are to dilate the small vessels in skeletal muscle and to increase cardiac output. Azapetine (Ilidar) hydrochloride is a dibenzasepine adrenergic blocking drug. It has been described as being adrenolytic and sympatholytic, having direct vasodilating effect on arteries and having an epinephrine reversal property. Tolazoline (Priscoline) hydrochloride is related to both sympathomimetic amines and histamines. This drug is reported to act synergistically with epinephrine on the animal heart and to increase cardiac output. In addition, it supposedly is an adrenolytic and sympatholytic agent. Phenoxyisopropylnorsuprifen (Drug 5029) is a European product. Reports on this drug indicate that its properties and structure resemble those of nylidrin hydrochloride.

Fifteen patients with peripheral vascular diseases underwent detailed laboratory studies before, during, and after infusions of the 4 vasodilators. None of the drugs showed consistently good results in all types of vascular diseases. The responses varied not only between persons with similar diseases but also from one extremity to another in the same person. Ilidar and Priscoline proved most effective in the majority of patients, especially as indicated by the detailed plethysmographic and temperature studies. There is excellent correlation between the effects of these drugs on the conjunctival vessels and the small vessels in the extremities, vessels that are easily accessible to photography in the testing of vasodilator drugs.

Vasodilator drugs that increase cardiac output must be administered with great caution in patients with heart disease. Additional studies on laboratory animals are indicated with regard to the effects of these drugs on the cardiac contractile force. It is postulated that each major system of arteries has its own "chemoreceptor mechanism," causing tremendous variations in the effects of vasoreactive drugs in different parts of the body at the same time.

Penicillin Treatment as Cause of Difficulties in the Diagnosis of Neurosyphilis. M. C. Mackenzie-Van Der Noordaa and F. M. Haagsma. Nederl. tijdschr. geneesk. **102**:1595-1597 (Aug. 16) 1958 (In Dutch) [Amsterdam].

When patients with neurosyphilis are treated with penicillin, the typical signs of dementia paralytica may disappear from the cerebrospinal fluid within a year, despite the fact that the patient's condition becomes progressively worse and the diagnosis of dementia paralytica has been confirmed. The authors observed this in 4 patients. If a patient has the clinical symptoms of dementia paralytica, although the spinal fluid does not show the characteristic changes, it should be borne in mind that a recent course of penicillin treatment may have masked the spinal fluid signs. Neurosyphilis is most likely to develop in patients who received inadequate or no treatment for their primary syphilitic infection. Therefore, penicillin

should never be given to patients who happen to have a positive Wassermann reaction, unless the spinal fluid has first been tested for evidence of neurosyphilitic changes.

Clinical Experience with Warfarin Sodium. M. Toohey. Brit. M. J. **2**:892-893 (Oct. 11) 1958 [London].

Warfarin sodium is a unique coumarin compound in that it can be given intravenously as well as by mouth. It has been stated that warfarin sodium is the "anticoagulant of choice." This paper describes observations on its use in 175 patients, most of whom had cardiovascular disease (myocardial infarction or cardiac failure) and the remainder had phlebothrombosis and pulmonary embolism. Treatment was controlled by the simultaneous use of Quick's and Owren's methods. A therapeutic level of between 2 and 3 times the normal control time (ideally 2½ times) was maintained when assessing results by Quick's method. For Owren's technique a level of between 10 and 14% was aimed at. Warfarin sodium was found to be a rapidly acting drug in that 95% of all patients reached a therapeutic prothrombin time in 36 hours. With daily doses of the drug just sufficient to maintain a therapeutic prothrombin time, the duration of action is approximately 36 hours. In large doses warfarin sodium has a sustained effect of up to 4 or 5 days. Therefore, large doses should be avoided. The usually recommended initial dose of 60 to 75 mg. proved far too much in this series; 35-to-50-mg. doses proved perfectly adequate for initial therapy, and it is inadvisable to exceed 50 mg. as an initial dose. The over-all average maintenance dose was 9 mg., and 80% of all patients were maintained on daily doses of between 5 and 15 mg.

Warfarin sodium proved extremely easy to control, and it probably ranks with phenindione as one of the 2 best anticoagulant drugs available for short-term therapy. Initial experience with warfarin sodium shows that it is also a useful anticoagulant for long-term therapy. In prescribing the anticoagulant, great care must be taken to allow for its cumulative effect. In this respect warfarin sodium resembles phenylpropyl-hydroxycoumarin, which has proved a reliable anticoagulant for long-term therapy. To obtain the best results with warfarin sodium, it is necessary to have available a strength of tablet with which to prescribe variations in dose of 0.5 mg. Scored 3-mg. and 5-mg. tablets would be ideal.

Clinical Evaluation of "Miradon." G. Kellaway. Brit. M. J. **2**:889-891 (Oct. 11) 1958 [London].

Since the introduction of bishydroxycoumarin (Dicumarol) a number of hydroxycoumarin and indanedione derivatives, causing depression of the prothrombin activity of blood, have become available for use as anticoagulants. They all suffer the disadvantage of being potentially dangerous and require frequent estimations of the prothrombin time for their control. The new anticoagulant, anisindione (Miradon), appears to be more rapidly effective than, and just as readily controlled as, any anticoagulant in current use. In previous tests on animals Miradon had given no evidence of toxicity. This report is concerned with its therapeutic use in 25 patients requiring anticoagulant therapy.

The initial response to a loading dose of 300 mg. was rapid, and some effect upon prothrombin time was evident in most subjects in 6 hours. More than 50% of the patients had prothrombin levels within the desired therapeutic limits (prothrombin activity of 10 to 20%) at 24 hours, and 86% of subsequent estimations of the prothrombin time were within similar limits. Normal prothrombin levels were recorded between 36 and 72 hours after cessation of treatment, and an even response was evident during therapy. Vitamin K_1 produced a rapid reversal of anticoagulant action. Compared with other anticoagulants, Miradon appears to approach more closely to the "ideal" for a short-term anticoagulant than any at present in common use. The uniformity of response to a single daily dose suggests that it would prove satisfactorily also in long-term therapy.

Contribution to Problem of Failure of Oral Therapy in Patients with Diabetes Mellitus. S. E. Strauzenberg, H. Haller and H. Meyer. München. med. Wchnschr. **100**:1535-1540 (Oct. 3) 1958 [Munich, Germany].

The authors report on 1,000 patients with diabetes mellitus who were treated with orally administered sulfonylurea compounds. From the beginning of their administration these drugs did not exert any effect on the carbohydrate metabolism of 202 (20.3%) of the 1,000 patients, who therefore were considered as primary failures. Twelve patients (1.2%) responded to the drugs for a short period ranging from 2 to 4 weeks, and after that the sulfonylurea compounds became rapidly ineffective; these patients were considered secondary failures. Seven hundred eighty-six patients were satisfactorily controlled by the sulfonylurea compounds for periods ranging from 6 to 8 weeks and also for much longer periods. The drugs then became ineffective in 33 (4.2%) of these 786 patients who were considered as genuine late failures. Not a single case of recent diabetes mellitus was observed among these 33 patients; the shortest duration of the disease was 2 years and the longest, 33 years.

No relationship was observed between age and body type of the patient and the incidence of late failure to respond to the sulfonylurea compounds. There was, however, a definite relationship between the incidence of such late failures and the quality

of the control of the carbohydrate metabolism by the sulfonylurea compounds. Of 448 patients who were easily and satisfactorily controlled with the aid of these drugs, 0.6% were late therapeutic failures, as compared with 7% of 280 patients who had shown only a moderate response to the drugs (with an abnormal daily amount of 10 to 20 Gm. of sugar in the urine) and 13% of 120 patients who had been unsatisfactorily controlled with the aid of these drugs (the abnormal daily amount of sugar in the urine varying from 20 to 30 Gm.). In this last group complete failure of response to the sulfonylurea compounds occurred most rapidly. These findings strongly suggest that prolonged therapy with sulfonylurea compounds should be limited to patients with the most favorable response to these drugs.

Late failure to respond to the sulfonylurea compounds is to be considered as a manifestation of the progressive course of the disturbance of metabolism, such as may be observed with similar frequency in other patients who had not been treated with sulfonylurea compounds. The fact that the metabolism can no longer be controlled with the aid of the sulfonylurea compounds is explained by the authors' concept of the mechanism of action of these drugs. According to this concept, the sulfonylurea compounds no longer exert an effect on the carbohydrate metabolism when the production of insulin in the patient's body is cut off to such a degree that a certain required amount of insulin is no longer available. The authors do not share the opinion of other workers that exhaustion of beta-cell activity may be caused by the sulfonylurea compounds.

Two Years' Experience with Viomycin Pantothenate Sulfate (Vionactan) in Treatment of Pulmonary Tuberculosis. G. F. Scalfi, P. Pontiggia and G. Rossa. Minerva med. 49:3343-3356 (Sept. 5) 1958 (In Italian) [Turin, Italy].

An Italian preparation, viomycin pantothenate sulfate (Vionactan), alone or in combination with other antibiotics, was administered to 48 male patients, between 19 and 49 years of age, with pulmonary tuberculosis for a period of 2 to 6 months. Vionactan was administered in a daily dosage of 2 Gm. every 2 or 3 days to 8 patients with chronic disease, who had been previously receiving other antibiotics for at least 2 years. Vionactan and isoniazid in a daily dosage of 5 mg. per kilogram of body weight were administered to the patients at the same time after it had been proved that the tolerance of the patients to Vionactan was good. Vionactan alone was given to another group of 13 patients. The daily dosage consisted of 1 or 2 Gm. of the drug given every other day for a period of 3 to 5 months. The early phases of pulmonary tuberculosis were present in 4 patients. Vionactan brought about radical improvement in 2 patients and marked improvement in 2. [By "radical improvement" is meant a substantial retrogression of the roentgenographic shadows; by "marked improvement" is meant a retrogression of exudative processes and shrinking of cavities.] The chronic phase of the disease was present in 9 patients. Vionactan therapy resulted in slight improvement in 2 patients; there was no change in 2 other patients, and the condition of 2 became worse.

A combination of Vionactan and other antibiotics was given to 35 patients. Twenty patients (including 8 patients of the first group) received orally the combination of Vionactan and isonazid. Slight improvement resulted in 5 patients, marked improvement in 9, and radical improvement in 3; there was no change in 3 patients. The combination of Vionactan and aminosalicylic acid was administered by intravenous infusion to 13 patients. It brought about slight improvement in 2 patients, marked improvement in 5, and radical improvement in 2; there was no change in 4 patients. The combination of Vionactan and streptomycin was given to 2 patients. It resulted in slight improvement in one patient and no change in one. The patients tolerated Vionactan very well. A slight degree of albuminuria developed in all the patients, being the only observed sign of renal reaction to the drug. Headache and vertiginous disorders attributed to the 8th cerebral nerve were noted in 2 patients. Vionactan combined with either isoniazid or aminosalicylic acid gave excellent results in patients in the early phase of pulmonary tuberculosis, who had not previously received or had received only a small amount of other antibiotics. This combination gave good results in patients with chronic disease who had not previously received any chemotherapy, and it gave fair results in those chronically ill patients who had previously received other antibiotics. The authors suggest that Vionactan combined with either isoniazid or aminosalicylic acid can be usefully employed for the treatment of the early phase of pulmonary tuberculosis, or the chronic phase without previous chemotherapeutic treatment, whereas the combination with streptomycin and other antibiotics can be left for succeeding therapeutic management requiring a prolonged maintenance therapy.

Clinical Experiences with the New Broad-Spectrum Antibiotic Reverin Injected by Intravenous Route. K.-F. Albrecht. Chirurg 29:445-448 (Oct.) 1958 (In German) [Berlin].

Reverin is the trade name given to a German preparation, pyrrolidinomethyltetracycline, which was developed by partial synthesis from pure tetracycline. This new tetracycline derivative shows in physiological pH areas a definitely improved solubility as compared with other tetracycline deriva-

tives. The strength of its action and the broadness of spectrum are exactly equivalent to those of tetracycline hydrochloride. At the surgical clinic of the University in Marburg on the Lahn (Germany) this new broad-spectrum antibiotic was given by intravenous route to 174 either hospitalized or ambulatory patients. Some of these patients had inflammatory conditions, such as furunculosis, suppurative bursitis, empyema of joint cavities, osteomyelitis, diabetic gangrene, peritonitis after perforating appendicitis, perforation of stomach, ileus, acute pancreatitis, and pneumonia, or urologic infections (to the exclusion of those caused by Proteus organisms and Pseudomonas aeruginosa). Other patients with paraurethral abscesses, surgically removable sequestrums, phlegmons of the palm, and paronychia received Reverin as an adjuvant to surgical therapy. The drug was also administered in intracranial operations, surgical intervention on pharyngoesophageal diverticula, gastrointestinal resections, cholecystectomy, prostatectomy, mastectomy, recurrent hernia operations, ureteral bougienage, removal of renal and ureteral calculi, cystectomy, and urologic plastic operations, as well as in fractures of the base of the skull, for prophylaxis of infections.

In most of these patients one intravenous injection of 275 mg. of Reverin daily for 4 to 7 days was sufficient for therapeutic and prophylactic purposes. Patients with severe infections or with those caused by pathogenic agents with reduced sensitivity to tetracycline were given 2 daily injections, and occasionally 4 or 5 daily injections were given. One intravenous injection of 5 to 25 mg. per kilogram of body weight proved to be sufficient in children. The satisfactory local tolerance of the drug made it possible to perform the intravenous injection within one minute. The resulting high initial concentration in the serum of the patient is apparently of essential clinical significance. Signs of irritation were not observed in the veins even with repeated injections made into the same blood vessel. No undesirable side-effects were observed except for insignificant sensations of bitter taste on the tongue which occurred in 70% of the patients.

PATHOLOGY

Copper Metabolism in Nor.aal Adults and in Clinically Normal Relatives of Patients with Wilson's Disease. F. C. Neale and M. Fischer-Williams. J. Clin. Path. 11:441-447 (Sept.) 1958 [London].

Increased copper content of the liver, brain, and other tissues, increased urinary excretion of copper, a decreased level of copper in the serum, and an associated decreased level of the copper-containing plasma protein coeruloplasmin are some of the biochemical abnormalities that are found in hepatolenticular degeneration (Wilson's disease). Aminoaciduria, not necessarily accompanied by an abnormal blood level of amino acids, is also found in hepatolenticular degeneration. This familial disease is inherited in a recessive, autosomal way. Biochemical abnormalities have occasionally been reported in clinically normal relatives of patients with hepatolenticular degeneration, namely, an excess aminoaciduria and a low coeruloplasmin level. The authors investigated the serum level and the urinary excretion of copper in 48 clinically unaffected relatives of patients with hepatolenticular degeneration.

The copper values obtained in serum and urine in these 48 persons are reported together with a control study of 106 normal adults. The urinary copper excretion was normal in all the relatives. The mean value for serum copper was found to be 100 mcg. per 100 ml. in normal males and 108 mcg. per 100 ml. in normal females, and this sex difference is statistically significant. Interpreted in the light of these control values, 35 of the 48 relatives had normal serum copper levels. Two child-bearing relatives showed high values. The parents of patients with hepatolenticular degeneration may be biochemically normal or abnormal. Eleven asymptomatic relatives showed low serum copper levels, and 5 of these were undoubtedly abnormal (47 to 70 mcg. per 100 ml.). Since half of these relatives were beyond the age at which hepatolenticular degeneration manifests itself, it may be concluded that some of the unaffected relatives have abnormally low serum copper levels.

Cutaneous Petechiae in Fatal Coronary Artery Disease. L. M. Gerlis. J. Clin. Path. 11:391-395 (Sept.) 1958 [London].

In the clinical recognition of myocardial ischemia, the nature and distribution of the referred pain which frequently accompanies it are of considerable diagnostic importance. Unfortunately in cases of sudden death there may be no such history, and not always is an unequivocal fatal cardiac lesion found, such as a recent or ruptured infarct or an acute occluding lesion of a coronary artery. In some there is little to indicate why or how the patient actually died, as the only cardiac lesions found are of long standing. In 7 autopsies in cases of acute coronary death, cutaneous petechiae were observed at sites commonly associated with referred pain of cardiac origin. No such lesions were observed in any deaths not of coronary origin. These petechiae were all outside the area of cutaneous postmortem hypostasis, and in no case was there any evidence of generalized hemorrhagic disease. It is suggested that this sign may be of diagnostic significance in the postmortem diagnosis of coronary insufficiency.

In the first patient presented, a 72-year-old woman, who died in a collapsed state with dyspnea and pain in the left shoulder 3 weeks after she had ex-

perienced an attack of gripping pain in the retrosternal region, autopsy revealed fine recent petechiae over the deltoid region and in the submammary region on the left side. The heart showed extensive recent infarction. Autopsy on another patient revealed a localized area of fine recent petechiae on the right side of the chest extending as a horizontal band, 7.5 cm. long and 5 cm. wide, just below the right nipple and fading out over the right border of the sternum. In still another patient small recent petechiae were seen over both shoulders and between the shoulder blades.

Two of the 7 patients had been subjected to frequent clinical examinations before death, but in neither case had cutaneous petechiae been noticed, nor have similar lesions been recorded among the clinical manifestations of coronary disease. Although fatal coronary disease is common, these petechiae are rare. Five of the 7 cases were from a personally studied series of 360 deaths due to coronary insufficiency in which a search for petechiae was specifically made, giving an incidence of 1.7%. These cutaneous petechiae may be caused by intense efferent stimuli along a sympathetic nerve pathway similar to that involved in referred pain, possibly by agonal relaxation of blood vessels which had been damaged by prolonged spasm. It is suggested that the presence of such localized petechiae is supporting evidence of acute coronary insufficiency, particularly in those cases in which the coronary arteries themselves show no recent culpable organic lesion. In 4 of the cases hemorrhagic lesions were found in direct relationship to the coronary arteries.

Simplified Technique of Cytodiagnosis in Cancers of the Esophagus: The "Wick" Procedure. C. Debray, J.-P. Hardouin, A. Deporte and E. Martin. Presse méd. **66**:1451-1452 (Sept. 24) 1958 (In French) [Paris].

The somber prognosis of esophageal cancer and the seriousness of the therapeutic measures it requires make it essential to establish the diagnosis by histological study. Esophageal biopsy and cytodiagnosis, the diagnostic methods now in use, have certain disadvantages. Thus, esophageal biopsy often produces negative results, because, for one reason or another, the specimen was not correctly obtained, while cytological diagnosis as usually practiced by lavage of the lesion uses large quantities of fluid requiring special centrifuges and necessitates the examination of a great number of slides. These disadvantages are overcome by a simplified method involving examination of cells deposited by contact on a rough fabric—that of a cotton wick.

The originality of the wick method lies in the manner in which the specimens are obtained. An ordinary oil-lamp wick with a diameter just large enough to fit over a Camus sound is sterilized and fastened in place over the sound, close to the knob, with a few twists of linen thread. The patient, who must be fasting, is given a preliminary injection of promethazine, and the prepared sound is introduced gently, and usually without difficulty, into the esophagus until it reaches the stenosis. The whole procedure is managed under radioscopic control. The sound is then advanced through the stenosed segment with special care to avoid false routes or perforations. Sometimes the passage can be accomplished easily; sometimes the patient must help to carry it out by expedients such as turning or swallowing a little water, or an injection of atropine may be given; sometimes, again, the attempt must be abandoned, because in no case should force be used. When the stenotic area has been cleared, the patient lies down for an hour during which the sound, with its wick, remains in contact with the lesion. It is then withdrawn; the wick is slit lengthwise and laid out flat; and specimens of the adherent film of mucus are removed for study. The material is usually abundant and can easily be analyzed after Papanicolau staining. Several specimens must be taken, however, because the cells found, even in one lesion, will vary according to the area from which they were obtained. Thus, red blood cells will appear predominantly in one slide, inflammatory elements in another, and, finally, cancer cells in a third.

Utilization of this technique produced positive results in 12 of 18 patients with cancer and negative results in 6 with non-neoplastic lesions. The 6 failures were due in 3 cases to failure of the sound to clear the stenotic area—in one, to a technical error by which the cells failed to adhere to the slide; in one, to the fact that the cells were necrotic and could not be analyzed; and, finally, in one, to the fact that the cancer was submucosal and there was no change in the mucosa. The wick procedure was, therefore, successful in 86% of the cases in which the stenotic area was satisfactorily cleared, excluding the one last mentioned in which there were no mucosal changes.

Myocarditis with Endocardial Elastomyofibrosis (EEMF). E. R. Fisher and E. R. Davis. Am. Heart J. **56**:537-552 (Oct.) 1958 [St. Louis].

The authors report on a 23-year-old Korean war veteran with myocarditis associated with severe endocardial elastomyofibrosis who died of cardiac failure about one year after the onset of the heart disease. Laboratory studies revealed a leukocytosis of 20,000 leukocytes per cubic millimeter, with 60% eosinophils, an elevated erythrocyte sedimentation rate, and hypochromic anemia. Ancylostoma and Ascaris ova were identified by stool examination, and a Trichinella skin test was positive on one occasion. There was a slight elevation of temperature to 100 F (37.8 C). In the earlier part of the patient's

illness electrocardiograms revealed nonspecific changes of T wave and QRS complex suggestive of pericarditis, but roentgenograms of the chest appeared normal. Electrocardiograms obtained before the patient's death revealed right axis deviation and digitalis effect, and chest roentgenograms obtained at this time showed marked cardiac enlargement and pulmonary congestion. The patient failed to respond to diuretics, digitalis, and supportive measures, and bilateral superficial venous femoral ligation did not alter the ingravescent course.

Autopsy showed that the entire endocardial surface of the inflow tract of the left ventricle, including two-thirds of this chamber, was thickened. The most caudal portion appeared greenish-gray and rugose. The papillary muscles were indistinct in the area of endocardial thickening. The entire circumference of the inflow tract of the right ventricle was also thickened. A circular defect was observed in the muscular portion of the interventricular septum. Marked luminal narrowing due to atherosclerosis was focally evident in both coronary arteries. Microscopic examination revealed focal interstitial myocardial fibrosis in many areas, particularly about the vessels. Interstitial inflammatory infiltrates, comprised principally of eosinophils, were not infrequent. Sections at the inflow tract of the left ventricle revealed superficial fibrinous layers subtended by collagen and numerous dilated vascular channels. Sections observed from the foci of endocardial thickening in the right and the left ventricle revealed much elastic tissue hyperplasia. Sections of the coronary arteries revealed the lumens to be eccentric due to marked intimal fibrosis and collections of foam cells and cholesterol clefts.

The clinical course and the anatomic features of the patient closely paralleled those described in that form of heart disease most frequently, but not exclusively, observed in Africa and designated by other workers as endomyocardial fibrosis or Löffler's endocarditis fibroplastica parietalis. In addition, severe atherosclerosis of the coronary arteries was present; this latter condition is considered to be pathogenetically, but not etiologically, related to the observed cardiac alterations. The patient's clinical history, infestation with Ascaris, Ancylostoma, and possibly Trichinella organisms, as well as the findings of blood eosinophilia and eosinophilic myocarditis, are considered strongly suggestive of the parasitic nature of the myocarditis, despite the failure to demonstrate such organisms within the heart. Although it is recognized that various causal factors may contribute to this type of heart disease, it is proposed that parasitic myocarditis may be more frequent in this regard than was previously appreciated, particularly in patients with eosinophilia. The primacy of myocardial damage in producing the endocardial alteration observed is emphasized, and the latter is attributed to both reparative and mechanical phenomena. The relationship of this apparently singular group of rare cardiac disorders to some recorded cases of idiopathic cardiomegaly and adult forms of so-called congenital fibroelastosis remains to be demonstrated.

Observations Concerning the Pathogenesis of Endocardial Thickening in the Adult Heart. E. R. Fisher and E. R. Davis. Am. Heart J. **56**:553-561 (Oct.) 1958 [St. Louis].

The authors report autopsy findings on the hearts of 109 unselected men, between the ages of 26 and 90 years, who died of various diseases. Varying degrees of endocardial thickening were observed in 66 of the 109 hearts: it was considered mild in 37, moderate in 23, and severe in 6 (the condition was not found in 43 hearts); and it was 6 times more frequent in the left than in the right ventricle. Microscopic examination revealed 2 types of endocardial thickening. The type considered as reparative was characterized by fibrosis with little or no proliferation of elastic tissue or smooth muscle; it was observed most frequently in association with major and minor myocardial infarction and the organization of mural thrombus. The compensatory or mechanical type appeared as a hypertrophy of smooth muscle and hyperplasia of the endocardial elastic fibers; the latter finding prompted the authors to designate this type of endocardial thickening as "endocardial elastomyofibrosis (EEMF)". Severe degrees of myocardial fibrosis appeared more closely related to cardiac hypertrophy and dilatation than to the age of the patient or to other factors investigated.

Endocardial elastomyofibrosis was most frequently observed in the outflow tract of the left ventricle; severe forms were observed with equal frequency at this site, as well as throughout this chamber. Since there was little indication that mild degrees of endocardial elastomyofibrosis were related to cardiac hypertrophy and dilatation, it is suggested that the latter may only accentuate this phenomenon. Other factors, such as the anatomic structure of the inflow tract and the "trauma" of ejected systolic blood, appear tenable as playing some part in the occurrence of endocardial thickening at this site.

PHYSIOLOGY

The Individuality of Nuclear Chromatin with Particular Reference to Polymorphonuclear Neutrophil Leukocytes. D. K. Briggs. Blood **13**:986-1000 (Oct.) 1958 [New York].

The essence of the sexual dimorphism of leukocytes is the presence or absence of drumsticks. These are stalked, rounded appendages of chro-

matin, 1.5 μ in diameter, projecting from the nuclei of the leukocytes of female subjects only. By counting the number of cells bearing the drumstick, it has been possible not only to divide patients into male and female but also to divide females into groups in terms of their drumstick counts. During the original investigation of chromatin sex in normal and abnormal individuals, it was found that the number of drumsticks possessed by different female subjects was widely variable. In order to derive some idea of the normal range of the drumstick count, studies were made on 100 student nurses. Their ages ranged from 18 to 30 years. The slides were made at the same time as blood was taken for hemoglobin measurement.

There are difficulties inherent in any method that attempts to enumerate the number of drumsticks per 500 leukocytes. It has been said that the drumstick is found on the nucleus of the mature leukocyte, but since it is difficult to decide at what point a leukocyte reaches maturity, all neutrophils including stab forms and juveniles were counted. This produced an unusually low drumstick count in comparison with what would have been obtained if the less mature forms had not been included. Another difficulty arises from uncertainties in recognizing a drumstick. The classical drumstick with its rounded head and narrow stem is never the source of error, but an appendage may be disguised when it lies close to the main body of the nucleus, has a short neck, or is otherwise deformed. Nevertheless, there was a high degree of reproducibility of counts made by different observers on the same blood smear or by the same observer on different occasions. The lowest counts amounted to 1 drumstick per 500 cells and the highest, 29 drumsticks per 500 cells. In order to determine how much this variation was due to the intrinsic error of the counting method and how much to individual conditions prevailing in each woman at the time of the examination, the counts were repeated for the 5 women showing the fewest drumsticks and the 5 showing the greatest number. In order to determine how much the drumstick counts were dependent upon factors operative at a particular time, all 10 women were recalled 6 months after the first examination, and further smears were made.

Later an attempt was made to determine what it was that distinguished the women who fell into the low drumstick count category from those in the high. The women were interviewed and their medical histories reviewed. They were assessed from various standpoints, such as age, racial background, and physical development. The author was unable to find any other single factor which was consistently different between the 2 groups. It is reasonable to suppose that the drumstick count, like a person's height or weight, is the product of many interrelated factors. If the 2 groups of women differ qualitatively from one another, then this distinction is as obscure as any clinical distinction which may exist between women of blood group A and those of group B. None has yet been found. In the case of blood groups, hereditary factors are of importance. The author is now investigating the drumstick counts of the mothers and sisters of some of the women who had persistently high or low drumstick counts.

Sex Differences in Plasma Fibrin, Fibrinolytic Capacity and Lipids as Influenced by Ingested Fat, Gonadectomy and Hormone Implants: Possible Implications for Pathogenesis of Coronary Occlusion. T. Gillman, S. S. Naidoo and M. Hathorn. Clin. Sc. **17**:393-408 (Aug.) 1958 [London].

The plasma fibrin and fibrinolytic activity, chylomicronemia, and blood lipids were studied intact, gonadectomized and hormone-treated gonadectomized male and female rats under basal conditions and 3 hours after a standard fat meal. Some preliminary findings in calciferol-treated rats are also reported. Basal blood lipids were almost identical in normal and gonadectomized rats; after fat ingestion the highest values were noted in male castrates. In male rats more marked chylomicronemia was found to develop than in females, at comparable total blood lipid values. This response to fat ingestion was shown to be influenced both by gonadectomy and by implanting testosterone or estradiol pellets into gonadectomized males and females. It is suggested that this greater chylomicronemia in male rats and in some of the hormone-treated gonadectomized rats may perhaps be due to differences in the mechanisms for clearing particulate lipid from the circulation and especially of reticuloendothelial activity in this regard. Basal fibrin levels were greater in intact males than females. Gonadectomy was followed by significant elevation of basal fibrin in females but not in males. Fat ingestion resulted in increases in plasma fibrin levels in most groups of rats here studied. Estradiol and testosterone pellet implantations were followed by elevations in plasma fibrin levels in gonadectomized males and females. The rise was particularly marked in testosterone-treated male castrates.

While plasma fibrinolytic activity was not found to differ significantly in male and female rats under basal conditions, it was noted that both fat ingestion and castration were followed by significant falls in males. Hormone implantation was followed by small changes in male castrates, but in spayed females testosterone produced considerable elevations, while estradiol decreased basal plasma fibrinolytic activity. Preliminary studies in rats with vascular and other injuries induced by toxic doses of calciferol showed that this treatment was followed by increases in basal plasma fibrin in intact

males and especially in castrates, with little or no change in testosterone-treated castrates. The fibrinolytic activity in the latter rats and in intact males was unchanged, while in untreated castrates the values fell almost to zero.

In commenting on possible implications of these findings, the authors suggest that the observation that fibrinolytic activity is lowered after the ingestion of fat is in keeping with the widely recognized high incidence of coronary occlusion among people with a high dietary fat intake. Studies of plasma fibrin and fibrinolytic activity, and their modification by sex hormones and dietary fat, are indicated in patients with coronary occlusive disease. If findings similar to those reported in rats are elicited in such patients, then the theory outlined elsewhere as to the possible interrelations of several factors (including vascular injury and repair, chylomicron clumping, blood sludging and coagulability as affected by sex and fat intake as well as reticuloendothelial activity) in the pathogenesis of coronary pathology, on the one hand, and of occlusive episodes, on the other, may provide a new and heuristically valuable approach in elucidating the etiology, prophylaxis, and perhaps even the treatment of coronary occlusive disease in man.

PUBLIC HEALTH

A Widespread Epidemic of Typhoid Fever Traced to a Common Exposure. W. A. Neill, J. D. Martin, E. A. Belden and W. Y. Trotter. New England J. Med. **259**:667-672 (Oct. 2) 1958 [Boston].

A widespread typhoid epidemic resulted from common exposure of the participants in a religious conference at MonArk Springs, Mo., in July, 1956. From field work done by local, state, and Public Health Service investigators, complete records were obtained on 373 of 405 known attendants from Missouri and Oklahoma (75% of the total attendance) and all patients with typhoid. Two-thirds of these persons experienced one or more intestinal illnesses during or shortly after the camp meeting. A sharp outbreak of diarrhea occurred during the first few days of the meeting. Illnesses continued to occur in smaller numbers throughout the meeting and for the next 4 or 5 weeks.

This typhoid epidemic is the most geographically widespread typhoid outbreak reported in the United States in which the source of infection has been traced by bacteriophage typing to the responsible carrier. Thirty-four cases of typhoid (one fatal) were discovered in 8 states. Seventeen of the 20 cases with positive culture were traced to the carrier of the same rare type of typhoid bacillus. During the 4 years previous to the MonArk Springs outbreak, this type (phage C-2) had been found in only 10 of 4,601 cases phage-typed in the United States. In addition to typhoid 2 diarrheal illnesses, distinguishable on the basis of incubation periods, were observed. The etiological agents were not discovered. Well water contaminated by the campers' sewage was the principal means of transmission of typhoid and diarrhea.

Asian Influenza Vaccine: Effect of Age and Schedule of Vaccination upon Antigenic Response. G. M. Bayne, O. C. Liu and W. P. Boger. Am. J. M. Sc. **236**:290-299 (Sept.) 1958 [Philadelphia].

Experience with other types of influenza has indicated that a 200 chick cell agglutinating (CCA) unit dose of vaccine, when given to a population without prior experience with the antigen, results in a relatively poor initial antibody response. This primary experience with the antigen may, however, make possible an adequate booster response to a second dose of vaccine given several months later. There was no information available to indicate that the optimal schedule for vaccination with the new monovalent 200 CCA unit Asian influenza vaccine was the same as that established for other strains. The studies described attempted to assess (1) the effect of a single-dose primary immunization upon antibody titer, (2) the effect of a 2-dose primary immunization upon antibody titer, (3) the efficacy of 1.0 ml. administered subcutaneously, compared with 0.1 ml. intracutaneously, in eliciting an antibody response, and (4) the effect of the age of the recipient upon the antibody response to vaccination.

The authors present data from a study of 312 persons relative to their antibody response to vaccination with a monovalent Asian influenza vaccine. These persons, as well as an additional 250 persons on a hospital staff who received this same lot of vaccine, were followed as regards side-effects. Less than 3% of these individuals exhibited significant local or systemic side-effects. Individuals over the age of 40 years, as a group, had a better response to a single-dose vaccination than did persons under the age of 40. A 2-dose immunization with a 4-week interval between doses was superior to either a single dose or 2 doses 2 weeks apart when a 200 CCA unit monovalent vaccine was employed. The intracutaneous route of inoculation was inferior to the subcutaneous route when the vaccine was given as a single injection to individuals without prior experience with the antigen. However, when it was administered as the second dose of a 2-dose immunization schedule with a 4-week interval, the intracutaneous and subcutaneous routes gave comparable responses. The availability of the Asian strain for incorporation into a polyvalent vaccine makes possible a considerably broader scope of protection against epidemic influenza.

BOOK REVIEWS

Physiological Bases of Psychiatry. Compiled and edited by W. Horsley Gantt, M.D. Part I from Pavlovian Laboratory, Johns Hopkins University, Baltimore. Director, W. Horsley Gantt. Part II from Behavior Laboratory, Cornell University, Ithaca, New York. Director, Howard S. Liddell. Publication number 323, American Lecture Series, monograph in Bannerstone Division of American Lectures in Objective Psychiatry. Edited by W. Horsley Gantt, M.D. Cloth. $10.50. Pp. 344, with illustrations. Charles C Thomas, Publisher, 301-327 E. Lawrence Ave., Springfield, Ill.; Blackwell Scientific Publications, Ltd., 24-25 Broad St., Oxford, England; Ryerson Press, 299 Queen St., W., Toronto 2B, Canada, 1958.

In May, 1955, at the 25th anniversary meeting of the Pavlovian Laboratory, headed and directed by W. Horsley Gantt, a series of papers was presented. At this meeting the Pavlovian Society was founded, and two years later held another meeting at the Behavioral Laboratory of Cornell University, directed by Howard S. Liddell. Both editors of this book are pioneers in the study of the Pavlovian concepts of conditioning in the United States. In Gantt's laboratory in the last 25 years about 300 papers have been published, all of which are listed in the back of this book under appropriate general headings. The book contains an adequate index to the published papers presented at the meeting. Some of these are old and are simply republished and others contain the data and conclusions from recent work. Not all of the papers presented at the 1957 meeting at Cornell are published in this volume, but it is anticipated that the rest will be contained in a subsequent book. The papers contained are not a summary of all of the physiological bases of psychiatry, much less all concerned with the problems of conditioning, so that the general title of the monograph is somewhat grandiose. Unfortunately the publisher took three and a half years after the presentation of the symposium to produce this work, and even the papers representing more recent work are already somewhat outmoded.

All in all, the book is a curious mixture containing introductory remarks by John Whitehorn, musings by Gantt, poetic fancies by Dos Passos, and a lengthy, redundant, highly speculative paper by Kempf. The general reader would gain little from this book that he could not obtain by following the literature. As a monument to Gantt's consistent work over the last 25 years and as a record of the beginning of the Pavlovian Society, it should be gratifying to the pioneers in research on conditioned reflexes.

These book reviews have been prepared by competent authorities but do not represent the opinions of any medical or other organization unless specifically so stated.

Head Injuries: Mechanisms, Diagnosis and Management. By E.S. Gurdjian, M.D., Professor of Neurological Surgery and Chairman of Department of Neurosurgery, Wayne State University College of Medicine, Detroit, and J. E. Webster, M.D., Associate Professor of Neurological Surgery, Wayne State University College of Medicine. Cloth. $14. Pp. 482, with 108 illustrations. Little, Brown & Company, 34 Beacon St., Boston 6; J. & A. Churchill, Ltd., 104 Gloucester Place, Portman Sq., London, W. 1, England, 1958.

This book reflects the extensive clinical, neurosurgical, and experimental experience of two neurosurgeons. It is well written and complete. The results of the study on mechanisms of injury and the interpretation of the results of the damage are particularly interesting. Diagnostic techniques are given in detail. The clinical manifestations are carefully portrayed. Complications and sequelae each occupy a complete chapter and a separate chapter is devoted to head injuries in infants and children. Both surgical and nonsurgical management are completely covered. This book should be available to every physician who treats head injuries.

The Practice of Nuclear Medicine. By William H. Blahd, M.D., Chief, Radioisotope Service, Veterans Administration Center, Los Angeles, Franz K. Bauer, M.D., Chief, Outpatient Service, Los Angeles County Hospital, and Benedict Cassen, Ph.D., Chief, Medical Physics Section, Atomic Energy Project and Clinical Professor of Biophysics, University of California at Los Angeles School of Medicine. Introduction by Paul Aebersold, Ph.D., Assistant Director for Isotopes and Radiation, Division of Civilian Application, United States Atomic Energy Commission, Washington, D. C. Foreword by Joseph F. Ross, M.D., Associate Dean, Professor of Medicine and Radiology, School of Medicine, University of California at Los Angeles. Cloth. $12.50. Pp. 407, with 112 illustrations. Charles C Thomas, Publisher, 301-327 E. Lawrence Ave., Springfield, Ill.; Blackwell Scientific Publications, Ltd., 24-25 Broad St., Oxford, England; Ryerson Press, 299 Queen St., W., Toronto 2B, Canada, 1958.

This work is divided into four parts which deal with physical principles underlying nuclear medicine, diagnostic methods involving the use of radioactive isotopes, therapeutic applications, and considerations of laboratory instrumentation and procedure. The first part contains instructive material that is likely to be new even to readers already familiar with the older literature of radiology. It includes a brief treatment of the intricate problems of dosimetry of the ionizing radiations. The second part begins with a detailed discussion of the use of iodine-131 in detecting abnormalities of form and function of the thyroid gland, and it continues with the various techniques used in localizing tumors, studying the gastrointestinal absorption of fats and proteins, testing the functions

of liver and gallbladder, detecting gastrointestinal hemorrhage by means of erythrocytes labeled with chromium-51, and recognizing abnormalities of cardiovascular and renal function. Three chapters are devoted especially to determinations of blood volume, the diagnosis of hematological disease, and the study of body composition by isotope dilution methods. The third part, on therapeutic applications, takes up the treatment of hyperthyroidism, euthyroid cardiac disease, and thyroid cancer with iodine-131, the treatment of hematological and malignant diseases with phosphorus-32, and the treatment of neoplastic disease with radiocolloids and with radiation from various internal and external sources. The last part is well supplied with floor plans, photographs of apparatus, tabular information, and other practical material of use in planning and operating a nuclear medicine laboratory. The book is commendable for the bibliographies at the end of each chapter and for a good index. It should be valuable as a reference work to students and specialists in radiology but should also interest any physician who wishes to see a panorama of nuclear medicine in its present state of development.

The Family Handbook of Home Nursing and Medical Care. By I. J. Rossman, M.D., Ph.D., Chief of Professional Services, Home Care Department, Montefiore Hospital, New York, and Doris R. Schwartz, R.N., Assistant Professor in Outpatient Nursing, Cornell University-New York Hospital School of Nursing, New York. Cloth. $4.95. Pp. 403, with illustrations. Random House, Inc., 457 Madison Ave., New York 22; Random House of Canada, Ltd., 1149 King St., W., Toronto 3, Canada, 1958.

A mine of valuable information, this volume is one of the more readable popular treatises on what one can do at home both to prevent and to care for illness. The authors emphasize the need for medical care and in great detail point out how to know when some member of the family needs a physician's services, how to locate a suitable physician, what to expect from the physician, and what the physician expects from both the patient and his family. Recognizing that most illnesses are cared for at home for all or part of their duration, the authors place special emphasis on the peculiar needs of each age group. An alphabetized appendix briefly describes home nursing techniques needed in the care of both bedridden and partially ambulant patients, suggests ways to make the nursing duties less exhausting, and indicates procedures on which the home nurse should receive instruction from the physician or the public health nurse. A particularly valuable part of this book is a simple, unemotional, and practical discussion of several major medical problems. These supplement the information the physician might give and stimulate questions for him to answer. Among these problems are infectious diseases, rheumatic heart disease, high blood pressure, heart attack, heart failure, stroke, arteriosclerosis and senility, ulcer, diabetes, arthritis, tuberculosis, mental illness, cancer, and diseases of the nervous system.

The practical approach to typical problems, the sincerity of the discussions on major illnesses, the forthright discussions of patient-physician relationships, and the absence of the usual "doctor book" flavor suggest this as an excellent book for physicians to recommend to families with children or persons chronically ill.

Eye Surgery. By H. B. Stallard, M.B.E., M.A., M.D., Surgeon, Moorfields Eye Hospital, London. Third edition. Cloth. $18. Pp. 899, with 671 illustrations. Williams & Wilkins Company, 428 E. Preston St., Baltimore 2; John Wright & Sons, Ltd., 42-44 Triangle West, Bristol 8, England, 1958.

The primary purpose of this new edition is to describe in detail surgical operative procedures which have been accepted in current practice. The chapters on anesthesia, corneal transplantation, the effect of radioactive disks in the treatment of intraocular neoplasms, and buried orbital implants have been extensively revised. Many of the older and classical plastic procedures, especially around the lids, have become obsolete and have been eliminated. Dr. Stallard is explicit in discussing many of the operations and gives his personal comments on those he prefers. A case in point is the anterior flap sclerotomy with basal iridencleisis selected by him as an effective operation for chronic glaucoma and relatively free from some of the unpleasant postoperative complications of some of the other operations used in the treatment of glaucoma. A unique feature of the book is the fact that the author has made all of his own drawings. Although on the whole they serve their purpose very well, some of them should have been larger and more explicit. This book should serve as an excellent reference work, particularly for younger ophthalmic surgeons.

Autopsy Diagnosis and Technic. By Otto Saphir, M.D., Pathologist, Michael Reese Hospital, Chicago. Foreword by Ludvig Hektoen, M.D. Fourth edition. Cloth. $8.50. Pp. 549, with 80 illustrations. Paul B. Hoeber, Inc. (medical book department of Harper & Brothers), 49 E. 33rd St., New York 16, 1958.

This book has become the standard American textbook on autopsy technique. It is, therefore, not surprising that a fourth edition has come out with some valuable additions. A few illustrations and comments have been added to various chapters, and the problem of unexpected deaths and legal examination receives more emphasis. The technique of autopsy of bodies containing radioactive isotopes is discussed, as well as autopsy tissue banking techniques. The new chapter on do's and don'ts gives evidence of the great experience of the author. The historical introduction by Dr. Sidney Farber is a pleasure to read. This book is well illustrated and well written.

QUESTIONS AND ANSWERS

SMALLPOX VACCINATION

To the Editor:—*The parents of a youngster have asked for an exemption from smallpox vaccination because of a severe reaction alleged to have occurred after a vaccination in September, 1952. The child has a history of a first vaccination in May, 1949, a second in September or October, 1949, a third in September, 1950, and the fourth in September, 1952. He has never had a "take." Four or five days after the last vaccination, he became ill with a high temperature, vomiting, and complaints of pain in the arm and shoulder. He had no headaches. It was advised never to let the child be vaccinated again, but the family has no written request of this type. Could the child have had a reaction due to vaccination and not have had a take? Would it be dangerous to vaccinate again?*

I. P. Barrett, M.D., Fort Worth, Texas.

Answer.—Complications after smallpox vaccination are mainly of the cutaneous type (pyogenic infection, eczema vaccinatum, or generalized vaccinia) or, far more rare, postvaccinal encephalomyelitis. They usually occur between 7 and 14 days after vaccination, and for their occurrence multiplication of the virus, i. e., a successful take, appears to be essential. In the particular instance to which the question refers, it is this consultant's opinion that the illness suffered by the youngster four days after vaccination was coincidental, since none of the symptoms of the above-mentioned complications were present. Consequently, there does not seem to be any reason for not vaccinating this youngster again. It is noted that repeated vaccination attempts have failed in this boy. Cases of smallpox have occurred in individuals in similar circumstances, meaning that failures to develop a primary take do not indicate immunity but are due to faulty vaccination techniques or to the use of vaccines which have lost their original potency because of improper or prolonged storage.

BACTERIAL HAPTENES

To the Editor:—*What is a bacterial haptene? What does it mean to "couple" a bacterial haptene to live cells? Any detailed information will be appreciated.*

M.D., Illinois.

Answer.—The term haptene was first used by Landsteiner in 1921 to denote substances which are incapable of stimulating antibody formation but which, when combined with a carrier molecule (e. g., a protein), will evoke antibodies and will impart specificity to them. The antibodies produced in this fashion will then be capable of reacting with the haptenes in some measurable way. It is now known that some of the complex haptenes can themselves induce antibody formation when injected intradermally or subcutaneously into certain animals. The bacterial haptenes are such haptenic substances occurring as components of many species of bacteria. The soluble specific substances present in the capsules of pneumococci are good examples of bacterial haptenes; they account for the type specificity of these organisms. Coupling means that the haptene is linked to a living cell by such means that the cell is not killed; the haptene serves to modify the immunological properties of the cell.

NEUTRON CAPTURE THERAPY

To the Editor:—*A patient, aged 42, has proved primary adenocarcinoma of the liver, and, as it involves most of the liver, it is inoperable. Is it possible that neutron capture therapy could be of value in such a case? If it offers any benefit, how and where could he receive such treatment?*

J. B. Eviston, M.D., Huntington, Ind.

Answer.—Neutron capture therapy, as first reported by Farr and others (*Am. J. Roentgenol.* **71**:279, 1954), is an experimental exploration of the possibilities of utilizing prompt, induced atomic disintegration to selectively destroy and thereby to control malignancy. Two components, one a target atom (thus far boron) and the other a thermal neutron derived from a nuclear reactor, interact with immediate disintegration of the boron atom into an alpha particle and an energetic lithium particle with both particles delivering up all their very considerable energy (2.4 mev) within a tissue volume approximately that of one cell. Selectivity is achieved by placement of the target atom through knowledge of its rate of distribution throughout the malignancy and the normal adjacent structures. With these data it is possible to utilize a neutron bath to flood the anatomic region with one component of the interacting couple (thermal neutrons), since the other component (boron-10) is chiefly distributed through the tissue to be destroyed during the time of neutron exposure. This procedure eliminates many problems of geometry inherent in external beam therapy. Since the specificity is achieved through proper utilization of time intervals after intravascular injection and vascular system distribution, the rates and magnitude of accumulation between malignant structures and surrounding

The answers here published have been prepared by competent authorities. They do not, however, represent the opinions of any medical or other organization unless specifically so stated in the reply. Anonymous communications cannot be answered. Every letter must contain the writer's name and address, but these will be omitted on request.

normal structures must be different enough to permit exposure to a requisite number of neutrons during this "safe" time interval. The presumed retarding effect of the blood-brain barrier made it possible to explore this procedure in relationship to glioblastoma multiforme by the Medical Department of Brookhaven National Laboratory. No patients have been cured, but results have been technically encouraging to the point of designing and now assembling a reactor specifically for medical purposes at Brookhaven and incorporation of a medical port facility in the new Massachusetts Institute of Technology reactor. While in principle the procedure might be useful in deep-seated malignancies in other organs of the body not otherwise susceptible to control, as yet technical difficulties have precluded exploration of any but the aforementioned brain tumor. Patients are considered for admission to Brookhaven National Laboratory Hospital by physician referral only. After extensive documentation and tissue specimens furnished by the referring physician have been studied by the Brookhaven National Laboratory staff to ensure appropriate patient qualification, the referring physician is advised of the decision regarding his patient. After treatment the patient is generally returned to the care of the referring physician.

PROPHYLACTIC SURGERY IN CANCER

To the Editor:—*Four sisters have died from metastasis of breast cancer within less than five years after radical mastectomy. All the lesions were found early. Their ages were 45 to 55 years at the time of death. There are three remaining sisters, aged 38 to 42 years. Would it be justifiable for these three sisters to have prophylactic bilateral simple mastectomy?*

Harold L. Bock, M.D., Stronghurst, Ill.

Answer.—The question posed of prophylactic surgery to avoid cancer in the presence of high familial incidence or of other seemingly predisposing factors has been frequently debated. Such a practice is not a generally accepted procedure. Although there is an occasional family in which all the sisters develop mammary cancer (this consultant knows of one such instance), it is quite a rare occurrence. Mastectomy is psychologically a traumatic experience. Its use on a prophylactic basis seems a little drastic. It might be pointed out that individuals who suffer from one cancer are more likely to develop another tumor than are members of the nontumorous population. A prophylactic mastectomy would not prevent the appearance of a tumor in another primary site. It is hoped that some of the new developments in oncology, such as the use of chemotherapy at operation as well as in the treatment of recurrent disease, will improve the prognosis for mammary and other tumors. Perhaps the living sisters need not suffer the same fate as the dead sisters even if they should be so unfortunate as to develop mammary cancer.

MUSCLE TIGHTNESS AND STRESS

To the Editor:—*With some variations, the following set of symptoms are rather often seen in this locality: aching of many muscles, with some soreness and tenderness on palpation or motion; joint pains; and more or less malaise. Physical examination usually shows normal findings. Occasionally, roentgenograms show a few arthritic spurs on some vertebral or other articular surfaces. Such patients are most often men of early middle age, although both sexes are affected; probably the most severely affected patient so far seen has been a farmer about 37 or 38 years of age. Cool wet weather makes the condition worse, and relief can usually be obtained temporarily by a trip to a different climate—almost any different climate. Perhaps the relief is obtained because of the incidental vacation from work and environment. Please comment.* *M.D., Illinois.*

Answer.—It seems likely that the patients described are suffering from the pain of muscle tightness brought on as a part of the bodily expression of emotional tension. The fact that freedom from responsibility, irrespective of climate, offers consistent relief to these patients would strengthen this inference. It is not widely appreciated that voluntary skeletal muscles may become involuntarily tense and display sustained contraction without the patient being aware of any increase in the contractural state of the muscles. Sustained contraction associated with a decrease in muscle blood flow has been shown to be productive of muscle pains and soreness in the muscles of the head, back, and extremities. It is not likely that the arthritic spurs have anything to do with the pain mechanism. The most effective treatment has been the one mentioned, that is, taking a breather with freedom from responsibility for a time. Reassurance and emotional support from the physician are also often helpful.

ANIMAL JAUNDICE AND INFECTIVITY OF MAN

To the Editor:—*What is the present conception of jaundice in animals? Is there a type of jaundice which is contagious to men? Is this type caused by virus and, if so, what kind of virus? It seems that there is a difference of opinion among veterinarians.* *M.D., Pennsylvania.*

Answer.—Animal jaundice may be caused by a number of infectious agents, as well as chemicals and poisonous agents. The question presumably refers only to the infectious types of jaundice or hepatitis which are caused by viruses, bacteria, protozoa, and helminths. The most common viral hepatitis is infectious canine hepatitis caused by Rubarth's virus. It has been described in all members of the canidae family and occurs widely in Europe, North America, and Australia—undoubtedly in most places where there is a sizable dog population. The virus of canine infectious hepatitis

is spread by direct contact among dogs. It is not infective for man. Other animals in addition to dogs are susceptible to viral hepatitis. The most important of these diseases is Rift Valley fever or infectious enzootic hepatitis of sheep and cattle. The disease was first described as appearing in British East Africa but now has appeared in Central and South Africa. It is highly contagious to man. It is spread to man by the handling of infected animals and their tissues. Mosquitoes may also transmit infection. The disease is almost never fatal in man. It resembles influenza or dengue. A viral hepatitis has been described in ducks in northern United States and England. This virus affects only young ducklings. No signs of disease appear in adult birds, although they are known to harbor the virus. A similar disease but unrelated antigenically has been described in chickens. The avian hepatitis is reported to be caused by a viral agent. Neither the duck's disease nor avian hepatitis virus are pathogenic for man. Leptospira infections are the most important bacterial cause of jaundice in animals. All domestic animals are susceptible to leptospirosis, as well as many rodents and wild animals. Most of these infections are communicable to man. Jaundice usually occurs with the rat type (caused by Lept. icterohaemorrhagiae) in man. The other animal Leptospira infections are usually characterized by meningitis in man. Other bacteria, as well as protozoa and helminths, may produce jaundice in animals, but these are usually the result of liver damage or blockage of bile ducts. Some of these agents may be communicable to man.

COLOR OF FRESHLY DRAWN BLOOD

To the Editor:—*Venous blood, drawn from a wide variety of persons, shows a rather wide range of color variation from near arterial red to a very dark red or near "black," as it will ordinarily be called. A tourniquet is always used to obtain the engorgement of the veins necessary to obtain the blood. The bright red venous blood has been obtained from children and the older the children the darker the blood; among adults, bright red blood is a rarity limited to a few muscular men of unusual vitality. While dark venous blood has always been observed in sickly adults, it has also been found in young adults without any obvious signs and symptoms of illness. Do these findings have any diagnostic significance?*

R. J. Kent, M.D., Savannah, N. Y.

Answer.—It is doubted that the color of freshly drawn venous blood has diagnostic significance. There are several factors which will influence the color of the blood: Anoxia due to inadequate aeration of the blood in the lung, heart failure, arteriovenous shunt, stasis, or prolonged constriction of the arm by the tourniquet will result in "dark blood" being withdrawn. A high hematocrit value will have the same effect. On the other hand, a low hematocrit value, high cardiac output without failure due to nervousness or thyrotoxicosis, drawing blood immediately after the placement of the tourniquet, or air in the syringe will yield "red" or "light" blood.

SALT INTAKE DURING PREGNANCY

To the Editor:—*An article by Robinson* (Lancet 1:178, 1958) *reports the administration of diets high in salt content to prevent or relieve most of the toxic phenomena of pregnancy, including early toxemia. The incidence of edema, perinatal death, and hemorrhage during and after pregnancy was recorded as lower in women taking extra salt. Is this not totally contrary to what has been the procedure, i.e., always to restrict the sodium or salt intake completely?*

Nat Kanner, M.D., Brooklyn, N. Y.

Answer.—Greenhill (Year Book of Obstetrics and Gynecology, 1957-1958, Chicago, Year Book Publishers, Inc., 1958, pp. 127-129) has commented that the article by Robinson is both disturbing and revolutionary "because most obstetricians throughout the world are afraid to use extra amounts of salt in pregnancy. In fact, most perfectly normal women in pregnancy are told to curtail salt ingestion. Certainly those who have any increase in blood pressure, proteinuria and edema are told to limit their intake. Now we are informed that extra salt in the diet seems to be essential for a healthy, pregnant woman and her baby. Many obstetricians, notably Dieckmann, have emphasized the dangers of salt during pregnancy. The following significant statements are from Dieckmann's book 'The Toxemias of Pregnancy' (ed. 2, St. Louis, C. V. Mosby Company, 1952, pp. 346-348): 'Excessive amounts of parenterally injected sodium chloride solution will produce edema, hypertension convulsions and coma in animals and human beings. . . . Several investigators state that some hypertensive patients placed on a low-sodium diet respond with a significant fall in blood pressure and the decrease is abolished by giving sodium chloride. . . . What was of greater interest to us was the increase in proteinuria which occurred in patients with pre-eclampsia after several injections of sodium chloride solution. . . . There would be as much as a 600 per cent increase within 24 to 48 hours and it would persist long after delivery.' Dieckmann also said (p. 353), 'It was surprising to note that of the patients who had been referred to the toxemia clinic because of hypertension, edema, proteinuria, or too rapid weight gain, 63 per cent showed no edema or no change in the degree of edema after the administration of sodium chloride or sodium bicarbonate. We were still more surprised when 12 per cent of the patients who had edema showed a decrease after the administration of sodium salt. It is noteworthy that of the 104 patients who received sodium salts, 31 per cent had no edema, 32 per cent had no change in the degree, 25 per cent had an increase of edema, and 12 per

cent a decrease in edema. These were all presumably abnormal patients that had been referred to the toxemia clinic, and yet in only 25 per cent was there a presumable association with sodium salts.'" Surely the relationship of salt intake to pregnancy, and particularly to the toxemias, requires elucidation.

NUTRITION FOR A PATIENT WITH TWENTY CENTIMETERS OF JEJUNUM

To the Editor:—*A patient underwent an extensive intestinal resection for regional ileitis. According to the operation records, only 20 cm. of small intestine was left below the ligament of Treitz, which was then anastomosed to the descending colon. The distal portion of the descending colon was brought out as a colostomy. This patient must maintain nutrition by absorption through the stomach, duodenum, 20 cm. of jejunum, and a short segment of descending colon. He has managed to keep alive for the past four years by feedings every few hours, made possible by the full-time attention of his mother. During this time, his nutritional state has gradually become worse, and he has been frequently hospitalized for blood transfusions. The hemoglobin level is 4 Gm. per 100 cc. and the red blood cell count a little over one million per cubic millimeter. Most of the food material comes through the colostomy unabsorbed. Can you give any suggestions as to feeding this patient?* *M.D., Louisiana.*

Answer.—This consultant cannot conceive of an operation for regional ileitis in which the whole small intestine, beginning 20 cm. below the ligament of Treitz, and the entire ascending colon are sacrificed, leaving a colostomy. Why should anastomosis of the jejunum to the mid-colon be done when it is assumed that the distal colon, sigmoid, and rectum were healed or normal? Why, then, the colostomy? A young man with 20 cm. of jejunum and a few centimeters of colon can expect his condition to worsen due to electrolyte imbalance and severe anemia. There is no way in which to reverse the situation, once this type of radical operation has been performed. Giving this patient high-calorie, high-vitamin, and high-protein diets is good. There are no predigested foods that have any great advantage over well-cooked, well-prepared foods at home, provided that the foods are slowly eaten and chewed well, with the meals prolonged. Canned baby foods are a favorite among such invalids, though it is not known whether they are of any great advantage. A concentrate protein, four to six tablespoonfuls a day, is a potent source of nitrogen nutrition. Only opium can slow the process of food through the small intestine, and that is not too desirable. Intravenous therapy should provide replacement of sodium, potassium, and calcium, and whole blood may be given as and when it becomes necessary—this will probably be very frequently.

PREGNANCY AND TUBERCULOSIS

To the Editor:—*A 32-year-old woman had tuberculous salpingitis bilaterally 12 years ago; this was treated with drainage through the vagina and with bed rest, without the use of antibiotics. She made a satisfactory recovery and has not had any pelvic symptoms since then. Six years ago she was treated for moderately advanced pulmonary tuberculosis with streptomycin and PAS (duration of chemotherapy, nine months). She recovered, and, at present, her chest x-ray is essentially normal with the exception of few small fibrous strands. Examination reveals moderate thickening of the right adnexa only; endometrial biopsy showed normal findings. Assuming that she could become pregnant, what are the possible risks? Could pregnancy reactivate her pelvic tuberculosis? In light of this history, could she anticipate other complications?* *M.D., Illinois.*

Answer.—Intrauterine pregnancy occurs very rarely in the presence of tuberculous salpingitis, active or healed (Schaefer, Tuberculosis in Obstetrics and Gynecology, Boston, Little, Brown & Company, 1956). The pregnancy itself usually is unaffected, but it may activate and cause the spread of the tuberculosis of the tubes. Healed pulmonary tuberculosis is rarely activated by pregnancy.

CELERY CONTACT DERMATITIS

To the Editor:—*A large number of severe dermatoses, consisting of erythema, edema, vesicles, and large bullae, have occurred in workers in celery fields. The lesions appear within 24 to 48 hours after contact. Celery farmers say that it is due to contact with pink rot, a fungus disease of the celery stalk. Please give further information on the disease, the offending agent, and suggested management.*

Robert Painter, M.D., Grant, Mich.

Answer.—Eczematous dermatitis caused by contact with celery was reported in 1926 by Legrain and Barthe in the French dermatological literature. Henry has published some interesting observations on "celery itch" among British cannery workers (*Brit. J. Dermat.* **45:**301, 1933; ibid. **50:**342, 1938). These investigators stated that contact dermatitis from celery is caused by the essential oil of the plant. According to Henry, this oil contains limonene, sedanolic acid, sedanonic acid, sesquiterpene, guaiacol, and palmitic acid. It was his opinion that limonene, common also to orange, lemon, bergamot, caraway, and dill, was the eczematogenic factor and that the eruption was the result of an "idiosyncrasy." None of these authors made specific reference to pink rot disease of the celery causing contact dermatitis, but Henry did state that several varieties of celery were handled and "that the pink was most 'pungent' and most likely to cause dermatitis." In this particular group of cases in Michigan,

the harvesters were afflicted. The description of the eruption as consisting of erythema, edema, vesicles, and large bullae correlates with an eczematous process of contact origin. It was not stated which areas were involved. Presumably, however, the hands, forearms, and perhaps the face and neck were involved. The rapid onset of the eruption within 24 to 48 hours suggests contact with a primary irritant substance. On the other hand, if the workers had been exposed previously to harvesting celery, the rapid onset could be based on an allergic response. Of equal consideration is the determination of whether the celery had been sprayed with a fungicide or pesticide containing an irritant and/or sensitizing chemicals a few days before harvesting. The future prognosis for these workmen is highly dependent on determination of these basic factors, because contact dermatoses caused by irritants can be prevented more readily with personal protective measures (gloves, sleeves, and/or barrier creams) than can allergic dermatoses.

BLOOD PRESSURE DETERMINATION AND VALVULAR DISEASE OF THE HEART

To the Editor:—*What would be the criteria for diagnosing hypertension in persons with those valvular diseases of the heart, such as aortic regurgitation, in which there is a decrease of the diastolic pressure? In cases of sclerosis of the mitral valve, where a characteristic, high-pitched systolic murmur, commonly called the sea gull murmur, is usually found, is there regurgitation?*

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Answer.—Little importance can be attached to high systolic blood pressures recorded at the periphery in the presence of free aortic valvular regurgitation associated with increased output needed to maintain systemic flow when there is a large reflux into the left ventricle. Systolic amplification of the arterial pulses in the peripheral arteries, as compared with central aortic pulses, is nearly uniformly shown through direct measurements in patients with this clinical syndrome. The diagnosis of true arterial hypertension must depend on other observations, such as the presence of retinal changes characteristic of hypertension. Although systolic pressures of 170 to 180 mm. Hg when the diastolic pressure approaches zero may be acceptable without associated hypertenion in young people, in older patients the presence of arterial sclerotic rigidity of the vessels will permit even higher systolic pressures without true hypertension being present. By common usage, the "sea gull" murmur, in a broad sense, has come to mean any high-pitched, screeching systolic murmur maximal near the cardiac apex. Whereas ordinarily this murmur is associated with mitral valve insufficiency, at times this type of murmur may be due to aortic valve stenosis, in which case the murmur is heard maximally over the left precordium. When this murmur is associated with mitral valve deformity, some degree of regurgitation must be presumed, even though this may be of such small quantity as to be of little or no hemodynamic significance.

CELIAC DISEASE SYNDROME

To the Editor:—*A child, aged 2, weighing about 18 lb. (8.2 kg.), has a celiac disease syndrome. Cystic fibrosis has been ruled out. The chief distressing symptoms include a chronic profuse nasal discharge and a marked susceptibility to upper respiratory diseases. Chest x-rays show essentially normal findings. The appetite is poor. The child has been on a diet for this condition, and meat, casein, bananas, and honey are some of the best-tolerated foods. About two weeks ago respiratory obstruction occurred, and the child was saved only by aspiration, bronchoscopy, and oxygen given for several days. Should prednisone be given for this condition? Please give other suggestions for treatment.* *M.D., Michigan.*

Answer.—The history of "a chronic profuse nasal discharge and a marked susceptibility to upper respiratory diseases" with a "celiac disease syndrome" in a child of this age and weight still sounds like cystic fibrosis. Furthermore, to be excluded are (1) allergy and (2) foreign body in the nares. There should be a minimum of exposure to respiratory infections, especially during winter months. Most helpful would be an entire winter spent in Arizona or the intermittent daily use of a bactericidal lamp in the child's room. Dust, smoke, drafts at night, iced foods, and kissing should be avoided. Maintenance of a relative humidity of 30 to 40% (airguide) and a room temperature of 65 to 72 F should improve the resistance of the upper respiratory mucous membranes, so that the child's ciliated epithelium functions at maximum capacity. Should allergy be an added factor, feather pillows and household pets (dog, cat, or bird) should be excluded from the child's environment. Daily doses of a polyvitamin should be given. At the onset of a respiratory attack, there should be absolute bed rest, increased moisture (50 to 60%), and properly spaced (around the clock), adequate, oral doses of an effective tetracycline given for several days; this dosage should then be gradually decreased. Should an attack increase in severity, especially if there is asthma or chronic bronchitis, prednisone should be given by mouth in a dosage of 1 or 2 mg. every four to six hours for 48 hours, with this dosage decreased by 1 or 2 mg. every few days and not administered longer than 7 to 10 days.